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L40          190 S L38 (L) L8
L41           27 S L40 AND (L11)
L42         1100 S L38 AND (PHARM?)
L43         1115 S L41 OR  L42
L44          456 S L38 (L) PHARM?
L45       153525 S PHARMACEU?
L46           11 S L40 AND L45
L47           27 S L46 OR L41
L48        29092 S (APROTIC OR DIPOLAR)/AB
L49            0 S L47 AND L48
L50         1646 S SECONDARY (L) SOLV?
L51         2096 S SECOND? (L) SOLV?
L52         1834 S (SECOND? (4A) SOLV?)/AB
L53         3790 S L52 OR L51
L54            0 S L47 AND L53
                  E APROTIC SOLVENTS/CT
                  E E3+ALL
                  E APROTIC SOLVENTS/CT
                  E E4+ALL
                  E E2+ALL
L55        10510 S L8 (L) (L17 OR L18 OR L20 OR L21 OR L22 OR L23 OR L24 OR
L38)
L56          647 S L55 AND (APROTIC OR APROTIC/AB)
L57           17 S L56 AND L11
L58           14 S L56 AND PHARMACEU?
L59           25 S L58 OR L57
L60           15 S L59 NOT L37

     FILE 'REGISTRY' ENTERED AT 08:17:00 ON 26 FEB 2001

     FILE 'HCAPLUS' ENTERED AT 08:17:51 ON 26 FEB 2001

=> d .ca 137 1-25;d .ca 160 1-15


L37  ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        2000:772593  HCAPLUS
DOCUMENT NUMBER:         133:309754
TITLE:                   Epimerization reaction for the production of racemic
                         fluoxetine by the reaction of enantiomerically
                         enriched fluoxetine(s) with a potassium counter-ion
                         base in an aprotic highly dipolar
                       solvent
INVENTOR(S):             Koenig, Thomas Mitchell; Mitchell, David
PATENT ASSIGNEE(S):      Eli Lilly and Company, USA
SOURCE:                  PCT Int. Appl., 13 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2000064855      A1   20001102      WO 2000-US6683   20000328
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
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ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-131074 19990426

AB The present invention provides a process for epimerizing the isomers of fluoxetine to the racemate by the reaction of enantiomerically enriched fluoxetine(s) (e.g., S-fluoxetine) with a potassium counter-ion base (e.g., KOH) in an aprotic highly dipolar solvent (e.g., DMSO).

IC ICM C07C213-10
ICS C07B055-00

CC 25-9 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): **63**

IT **Solvents**
(**aprotic**, highly dipolar; epimerization reaction for the prodn. of racemic fluoxetine by the reaction of enantiomerically enriched fluoxetine(s) with a potassium counter-ion base in)

IT Bases, uses
RL: CAT (Catalyst use); USES (Uses)
(epimerization reaction for the prodn. of racemic fluoxetine by the reaction of enantiomerically enriched fluoxetine(s) with a potassium counter-ion base in an **aprotic** highly dipolar **solvent**
)

IT Epimerization
(for the prodn. of racemic fluoxetine by the reaction of enantiomerically enriched fluoxetine(s) with a potassium counter-ion base in an **aprotic** highly dipolar **solvent**)

IT 865-47-4 1310-58-3, Potassium hydroxide, uses
RL: CAT (Catalyst use); USES (Uses)
(epimerization reaction for the prodn. of racemic fluoxetine by the reaction of enantiomerically enriched fluoxetine(s) with a potassium counter-ion base in an **aprotic** highly dipolar **solvent**
)

IT 100568-02-3, S-Fluoxetine 114247-09-5, R-Fluoxetine hydrochloride
RL: RCT (Reactant)
(epimerization reaction for the prodn. of racemic fluoxetine by the reaction of enantiomerically enriched fluoxetine(s) with a potassium counter-ion base in an **aprotic** highly dipolar **solvent**
)

IT 54910-89-3P, Fluoxetine
RL: SPN (Synthetic preparation); PREP (Preparation)
(epimerization reaction for the prodn. of racemic fluoxetine by the reaction of enantiomerically enriched fluoxetine(s) with a potassium counter-ion base in an **aprotic** highly dipolar **solvent**
)

IT **67-68-5**, Dmso, uses 68-12-2, Dmf, uses 98-95-3, Nitrobenzene, uses 100-47-0, Benzonitrile, uses 110-86-1, Pyridine, uses 126-33-0,
Sulfolane **127-19-5**, **Dimethylacetamide** 680-31-9, Hexamethylphosphoramide, uses 872-50-4, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(**solvent**; epimerization reaction for the prodn. of racemic fluoxetine by the reaction of enantiomerically enriched fluoxetine(s) with a potassium counter-ion base in an **aprotic** highly

dipolar **solvent**)
REFERENCE COUNT: 1
REFERENCE(S): (1) Rossetti, V; US 5847214 A 1998 HCAPLUS

L37 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:573546 HCAPLUS
DOCUMENT NUMBER: 133:149254
TITLE: Purification of lipstatin from microbial fermentation by solvent extraction
INVENTOR(S): Doswald, Stephan; Kupfer, Ernst; Steinbauer, Gerhard; Steinwender, Erich
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1028115	A1	20000816	EP 2000-101141	20000121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6156911	A	20001205	US 2000-491557	20000126
JP 2001039962	A2	20010213	JP 2000-16717	20000126
CN 1266058	A	20000913	CN 2000-101172	20000128
PRIORITY APPLN. INFO.:			EP 1999-101893	19990129

AB Crude lipstatin obtained from microbial fermn. is extd. from a non-polar solvent (e.g., aliph. or arom. hydrocarbon) into a polar solvent (e.g., carboxylic acid, alc., O-monosubstituted mono- or polyethylene glycol). The polar solvent phase is dild. with water, and lipstatin is re-extd. into a fresh non-polar solvent. The process may begin with extn. of oxidized methionyl lipstatin followed by hydrogenation of lipstatin to tetrahydrolipstatin and crystn. of tetrahydrolipstatin. Tetrahydrolipstatin is useful for prevention and treatment of diseases assocd. with obesity.
IC ICM C07D305-12
CC 16-1 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 9, **63**
IT **Solvents**
(**aprotic**, dipolar; purifn. of lipstatin from microbial fermn. by **solvent** extn.)
IT **64-19-7**, Acetic acid, uses 67-56-1, Methanol, uses 107-21-1D, Ethylene glycol, O-monosubstituted 109-86-4, Ethylene glycol monomethyl ether 142-82-5, Heptane, uses **25322-68-3D**, **Polyethylene glycol**, O-monosubstituted
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(purifn. of lipstatin from microbial fermn. by solvent extn.)
REFERENCE COUNT: 1
REFERENCE(S): (1) La Roche, H; EP 0803576 A 1997 HCAPLUS

L37 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:718963 HCAPLUS
DOCUMENT NUMBER: 131:327554
TITLE: Non-aqueous peptide formulations comprising non-aqueous protic solvents

INVENTOR(S): Stevenson, Cynthia L.; Tao, Sally A.; Prestrelski, Steven J.; Eckenhoffdeceased, James B.; Wright, Jeremy C.; Leonard, John J., Jr.
PATENT ASSIGNEE(S): Alza Corporation, USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5981489	A	19991109	US 1997-874680	19970613
US 6066619	A	20000523	US 1999-293172	19990416

PRIORITY APPLN. INFO.: US 1997-874680 19970613

AB This invention relates to stable non-aq. protic formulations of peptide compds. These stable formulations comprise peptide in non-aq. protic solvent. They may be stored at elevated temps. for long periods of time and are esp. useful in implantable delivery devices for long term delivery of drug. Formulations of 40% leuprolide acetate (I) in PEG:water (90:10) were prepd. and used to fill the reservoirs of implantable drug delivery devices. The filled devices were subjected to accelerated aging by storing them at elevated temps. (80-88.degree.) for seven days in an incubator. This is equiv. to about six months at 37.degree. or about one year at room temp. (25.degree.), assuming an activation energy (Ea) of 16.6 kcal/mol. These formulations were able to maintain the stability of I and in each case, at least 65% I was retained.

IC ICM A61K038-00
ICS C07K005-00; C07K007-00
NCL 514015000
CC **63-6** (Pharmaceuticals)
ST peptide formulation protic solvent; **pharmaceutical** implant leuprolide PEG stability
IT Polar **solvents**
(**aprotic**; non-aq. protic peptide formulations comprising non-aqueous protic **solvents**)
IT **56-81-5**, 1,2,3-Propanetriol, uses **57-55-6**, 1,2-Propanediol, uses **67-68-5**, Dmso, uses 68-12-2, uses 9004-74-4 **25322-68-3**
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(non-aq. protic peptide formulations comprising non-aqueous protic solvents)
REFERENCE COUNT: 35
REFERENCE(S): (1) Anon; EP 0312052 1989 HCAPLUS
(2) Anon; EP 0432479 1991 HCAPLUS
(3) Anon; EP 0510731 1992 HCAPLUS
(4) Anon; WO 9220711 1992 HCAPLUS
(5) Anon; WO 9406452 1994 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:483357 HCAPLUS
DOCUMENT NUMBER: 131:134637
TITLE: Non-aqueous polar aprotic peptide formulations

INVENTOR(S): Stevenson, Cynthia L.; Prestrelski, Steven J.
PATENT ASSIGNEE(S): ALZA Corp., USA
SOURCE: U.S., 16 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5932547	A	19990803	US 1997-874233	19970613
CN 1224358	A	19990728	CN 1997-196072	19970701
US 6124261	A	20000926	US 1999-293839	19990419
PRIORITY APPLN. INFO.:			US 1996-22699	19960703
			US 1997-874233	19970613

AB This invention relates to stable non-aq. polar aprotic formulations of peptide compds. These stable formulations comprise peptide in non-aq. polar aprotic solvents. They may be stored at elevated temps. for long periods of time and are esp. useful in implantable delivery devices for long term delivery of drug.

IC ICM A61K038-00
ICS C07K005-00; C07K007-00
NCL 514015000
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): 2, 8
ST peptide hormone storage nonaq **aprotic solvent**
IT Polar **solvents**
(**aprotic**; non-aq. polar **aprotic** peptide formulations)
IT **Solvents**
(protic; non-aq. polar **aprotic** peptide formulations)
IT **67-68-5**, Dmso, uses 68-12-2, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(non-aq. polar aprotic peptide formulations)
REFERENCE COUNT: 35
REFERENCE(S): (2) Anon; GB 2008403 1978 HCAPLUS
(3) Anon; GB 2119248 1983 HCAPLUS
(4) Anon; GB 2119248 1983 HCAPLUS
(5) Anon; WO 9220711 1992 HCAPLUS
(6) Anon; WO 9419020 1994 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:286179 HCAPLUS
DOCUMENT NUMBER: 130:316655
TITLE: Method for preparation of homogeneous, surface-active carbohydrate derivatives and anhydrous preparations containing polar and nonpolar substances
INVENTOR(S): Heidlas, Juergen; Wiesmueller, Johann
PATENT ASSIGNEE(S): SKW Trostberg A.-G., Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19733269	A1	19990429	DE 1997-19733269	19970801

AB Anhyd. formulations of polar or nonpolar substances are provided which are readily converted to mol. dispersions, microdispersions, or microemulsions by addn. of a solvent. These formulations are highly stable during storage at room temp. and are suitable for use in the food, biotechnol., agrochem., cosmetic, and pharmaceutical industries. The soly. or dispersibility of the formulation is controlled by the mol ratio of carbohydrate deriv. to active agent in the formulation, i.e. an excess of surface-active carbohydrate makes the formulation more lipophilic and facilitates dispersion or dissoln. of a polar active agent in oil. The formulation is prepd. by (a) dissolving the polar or nonpolar substance in an anhyd. polar solvent or solvent mixt., (b) mixing this soln. with a surface-active carbohydrate deriv. (optionally dissolved in a polar or nonpolar solvent) in a mol ratio of carbohydrate to active agent of 1:(0.01-1), (c) optionally adding an anhyd., hydrophilic polyol- or polyether-based excipient in a mol ratio of 1:(0.01-1) based on the carbohydrate, and (d) extg. the mixt. with a C2-4 hydrocarbon mixt. and/or Me2O in a column at 20-150.degree. and 3-50 MPa to produce a liq. top product contg. solvent and a bottom product contg. carbohydrate deriv. and polar or nonpolar active agent as an anhyd. homogeneous melt. Thus, 2 g chloramphenicol was dissolved in 50 mL EtOH at 50.degree. and the soln. was stirred into a molten mixt. of sorbitan monostearate 100 and refined soybean oil 20 g at 50.degree.. This mixt. was injected into the middle of an extn. column and extd. with liquefied propane; the temps. at the top, injection port, and bottom of the column were 98, 90, and 83.degree., resp., and the feed:propane ratio was 2.5 wt.%. EtOH and soybean oil were recovered from the top fraction; the bottom fraction, after evapn. of propane, comprised chloramphenicol and sorbitan monostearate in a mol ratio of .apprx.0.03.

IC ICM A61K009-10
ICS A61K007-00; A61K031-455; A61K031-575

CC **63-6** (Pharmaceuticals)
Section cross-reference(s): 17

IT **Aprotic solvents**
Disperse systems
Dyes
Extraction columns
Lacquers
Leather
Microemulsions
Microemulsions (drug delivery systems)
Polar molecules
Polar solvents
Powders (drug delivery systems)
Solvent extraction
Suspensions (drug delivery systems)
(method for prepn. of homogeneous, surface-active carbohydrate derivs.

and anhyd. prepns. contg. polar and nonpolar substances)
IT **Soybean oil**
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(solvent; method for prepn. of homogeneous, surface-active carbohydrate
derivs. and anhyd. prepns. contg. polar and nonpolar substances)

L37 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:141201 HCAPLUS
DOCUMENT NUMBER: 130:187177
TITLE: **Parenteral** pimaricin as treatment of systemic infections
INVENTOR(S): Andersson, Borje S.; Anaissie, Elias J.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9908663	A1	19990225	WO 1998-US16661	19980807
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6045815	A	20000404	US 1997-911607	19970815
EP 1007013	A1	20000614	EP 1998-939905	19980807
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1997-911607	19970815
			WO 1998-US16661	19980807

AB An antifungal compn. suitable for parenteral administration to a mammal includes an amt. of pimaricin or an antifungal deriv. thereof that is effective to inhibit the growth of a fungal infection on a mammal; a pharmaceutically acceptable dipolar aprotic solvent; and a pharmaceutically acceptable aq. secondary solvent. The compn. can be used in methods of preventing or treating a systemic fungal infection in a mammal. The compn. can be prepd. by dissolving pimaricin (I) or an antifungal deriv. thereof in the pharmaceutically acceptable dipolar aprotic solvent; adding to the soln. a pharmaceutically acceptable aq. secondary solvent; and in a preferred method, by subsequently lyophilizing the compn., whereby a dry, shelf-stable compn. is produced. This dry compn. can be reconstituted into an aq. soln. suitable for parenteral administration. I was sol. in glacial acetic acid and di-Me acetamide to at least 100 mg/mL. Parenteral formulations of I were prepd. and their stability was studied.
IC ICM A61K009-50
CC **63-5** (Pharmaceuticals)
ST **parenteral pharmaceutical** pimaricin systemic infection solvent
IT **Aprotic solvents**
Fungicides
Intravenous injections

Parenteral solutions (drug delivery systems)
(**parenteral** pimaricin as treatment of systemic infections)

IT Fatty acids, biological studies
Soybean oil
Vegetable oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**parenteral** pimaricin as treatment of systemic infections)

IT Infection
(systemic; **parenteral** pimaricin as treatment of systemic infections)

IT 7681-93-8, Pimaricin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**parenteral** pimaricin as treatment of systemic infections)

IT **127-19-5**, Dimethyl acetamide
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(**parenteral** pimaricin as treatment of systemic infections)

IT 50-99-7, Dextrose, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**parenteral** pimaricin as treatment of systemic infections)

REFERENCE COUNT: 3
REFERENCE(S):
(1) Andersson; US 5430057 A 1995 HCAPLUS
(2) Anon; Drug Information for the Health Care Professional USPDI Ninth Edition 1989, P1705
(3) Sugiyama; US 5651991 A 1997 HCAPLUS

L37 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:23310 HCAPLUS
DOCUMENT NUMBER: 130:158463
TITLE: Polyhydroxy ether resins, their membranes for artificial lung in open heart surgery, and their manufacture
INVENTOR(S): Fukuoka, Tetsuya; Tatehata, Hideki; Mochizuki, Akira
PATENT ASSIGNEE(S): Terumo Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 33 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11001554	A2	19990106	JP 1997-172834	19970613

AB Title resins comprise insol.-gel-free [OROCH2CH(OH)CH2]l [I; 20-100 mol% of R = p-C6H4C(CF3)2C6H4-p; other R = Q1-Q3, p-C6H4; X = SO2, CO, O, CH2, CHMe, CMe2, C[(CH2)nMe]2, CH(CH2)nMe, CH(CH2)nCHMe2, cyclopentylidene, (substituted) cyclohexylidene, CMePh, CPh2, fluorenylidene, p-CMe2C6H4CMe2; Y = H, halo, alkyl, alkoxy, Ph; l .gtoreq. 1; m = 1-4; n .gtoreq. 0], show reduced viscosity [at 25.degree. and 0.5 g/100 mL, in N,N-dimethylacetamide (II)] .gtoreq.0.6 dL/g, and are prepd. by reaction of bisphenols with epihalohydrins in aprotic polar solvents. The membranes, which show good plasma leakage resistance and gas permeability, are manufd. by dissolving I into DMSO, II, N-methyl-2-pyrrolidone, DMF, THF, Me2CO, and/or sulfolane in the presence of H2O, salts, low-mol.-wt. compds., or polymers and forming membranes by a dry-wet or dry method.

Bisphenol AF was polymd. with epichlorohydrin in a DMSO-II mixt. to give a polymer (reduced viscosity 0.6 dL/g, Tg 124.degree.), which was made into a membrane showing water contact angle 100.degree. and bovine plasma contact angle 105.degree..

IC ICM C08G065-28
ICS A61L027-00

CC **63-7** (Pharmaceuticals)
Section cross-reference(s): 35, 38

IT Polar **solvents**
(**aprotic**, in polymn.; prepn. of polyhydroxy polyethers as membranes for artificial lung)

IT **Aprotic solvents**
(polar, in polymn.; prepn. of polyhydroxy polyethers as membranes for artificial lung)

IT **56-81-5**, **Glycerin**, biological studies 57-13-6, Urea, biological studies **57-55-6**, **Propylene glycol**, biological studies 64-17-5, Ethanol, biological studies 67-56-1, Methanol, biological studies 107-21-1, Ethylene glycol, biological studies 111-46-6, Diethylene glycol, biological studies 7447-41-8, Lithium chloride, biological studies 7647-14-5, Sodium chloride, biological studies 7786-30-3, Magnesium chloride, biological studies 7791-03-9, Lithium perchlorate 9003-01-4, Poly(acrylic acid) 9003-05-8, Polyacrylamide 9003-39-8, Poly(vinylpyrrolidone) 10034-81-8, Magnesium perchlorate 10043-52-4, Calcium chloride, biological studies **25322-68-3**, **Polyethylene glycol** 25322-69-4, Polypropylene glycol 62309-51-7, Propanol
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(additive for membranes; prepn. of polyhydroxy polyethers as membranes for artificial lung)

IT **67-68-5**, **Dimethyl sulfoxide**, uses 68-12-2, N,N-Dimethylformamide, uses 109-99-9, Tetrahydrofuran, uses 123-91-1, Dioxane, uses 126-33-0, Sulfolane **127-19-5**, N,N-**Dimethylacetamide** 872-50-4, N-Methylpyrrolidone, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(polymn. solvent; prepn. of polyhydroxy polyethers as membranes for artificial lung)

L37 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:682154 HCAPLUS
DOCUMENT NUMBER: 129:306517
TITLE: Homogeneous water-free formulations containing glycerophospholipids and polar or lipophilic substances
INVENTOR(S): Heidlas, Juergen; Zirzow, Karl-Heinz; Wiesmueller, Johann; Graefe, Juergen
PATENT ASSIGNEE(S): SKW Trostberg A.-G., Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9843674 A1 19981008 WO 1998-EP1789 19980326
W: JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
DE 19758157 A1 19981001 DE 1997-19758157 19971230
EP 969871 A1 20000112 EP 1998-917090 19980326
R: BE, DE, FR, GB, IT, NL
PRIORITY APPLN. INFO.: DE 1997-19713093 19970327
DE 1997-19713094 19970327
WO 1998-EP1789 19980326
OTHER SOURCE(S): MARPAT 129:306517

AB Homogeneous, water-free formulations for the prepn. of dispersions, emulsions, and/or suspensions, which contain glycerophospholipids, polar or lipophilic substances (e.g. physiol. active substances) with an affinity for glycerophospholipids in a molar ratio to glycerophospholipids of (0.001-2):1, and optional water-free excipients (e.g. glycerin) in a molar ratio to glycerophospholipids of (0.001-1):1 are provided which form stable aggregates suitable for numerous areas of application, e.g. in food technol., biotechnol. or the pharmaceutical industry. Increasing the proportion of glycerophospholipids in the formulation increases its lipophilic character; on the other hand, the dispersibility or soly. of substances in water is increased by use of excipients (e.g. polyols). The formulation is produced from a soln. of the active substance in a polar or nonpolar solvent by adding a soln. of glycerophospholipids and optional excipients so that all components remain in soln., extg. with a volatile hydrocarbon in a column under elevated temp. and pressure, and removing the mixt. of formulation components from the bottom of the column as a melt, which is freed of the hydrocarbon solvent by reducing the pressure. Thus, a soln. of nicotinamide 5.1 in EtOH 84 was mixed at 45.degree. with 450 g of a 65:35 mixt. of soybean glycerophospholipids and soybean oil triglycerides. This mixt. was injected in the middle of an extn. column and extd. with compressed propane at 60 bar and 65-85.degree.; the triglyceride oil and EtOH were removed from the top of the column, and the essentially oil-free nicotinamide-glycerophospholipid formulation was withdrawn from the bottom and decompressed to allow propane to evap., leaving a pourable powder contg. 1.7 wt.% nicotinamide.

IC ICM A61K047-24
ICS A61K009-14
CC **63-6** (Pharmaceuticals)
ST **pharmaceutical** dispersion conc glycerophospholipid; food emulsion conc phospholipid
IT Agrochemical formulations
Antioxidants
Aprotic solvents
Biotechnology
Cosmetic emulsions
Dyeing
Dyes
Emulsions (drug delivery systems)
Extraction
Extraction columns

Food emulsions
Lacquers
Leather
Polar molecules
Polar solvents
Powders (drug delivery systems)
Solvents
Suspensions (drug delivery systems)
(homogeneous water-free formulations contg. glycerophospholipids and polar or lipophilic substances)

IT Glycols, biological studies
Lecithins
Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylglycerols
Phosphatidylinositols
Phosphatidylserines
Phospholipids, biological studies
Polyhydric alcohols
Soybean oil
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homogeneous water-free formulations contg. glycerophospholipids and polar or lipophilic substances)

IT **56-81-5, Glycerin**, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homogeneous water-free formulations contg. glycerophospholipids and polar or lipophilic substances)

L37 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:55545 HCAPLUS
DOCUMENT NUMBER: 128:132417
TITLE: Nonaqueous polar aprotic peptide formulations
INVENTOR(S): Stevenson, Cynthia L.; Prestrelski, Steven J.
PATENT ASSIGNEE(S): Alza Corp., USA; Stevenson, Cynthia L.; Prestrelski, Steven J.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800158	A1	19980108	WO 1997-US11450	19970701
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2259557	AA	19980108	CA 1997-2259557	19970701

AU 9735879	A1	19980121	AU 1997-35879	19970701
EP 921808	A1	19990616	EP 1997-932416	19970701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9710132	A	19990810	BR 1997-10132	19970701
JP 2000515131	T2	20001114	JP 1998-504401	19970701
NO 9806207	A	19990303	NO 1998-6207	19981230
PRIORITY APPLN. INFO.:			US 1996-22699	19960703
			WO 1997-US11450	19970701

AB This invention relates to stable nonaq. polar aprotic formulations of peptide compds. These stable formulations comprise peptide in non-aq. polar aprotic solvent. They may be stored at elevated temps. for long periods of time and are esp. useful in implantable delivery devices for long term delivery of drug. Examples are given for stability testing of peptides such as leuprolide acetate in nonaq. solvents such as DMF or DMSO.

IC ICM A61K038-04
ICS A61K038-08; A61K038-09; A61K038-24; A61K047-08; A61K047-16; A61K047-18; A61K047-20

CC **63-6** (Pharmaceuticals)

IT **Aprotic solvents**
Implants (drug delivery systems)
Parenteral solutions (drug delivery systems)
Solutions (drug delivery systems)
(nonaq. polar **aprotic** peptide formulations)

IT **Solvents**
(protic; nonaq. polar **aprotic** peptide formulations)

IT **67-68-5**, Dmso, biological studies 68-12-2, Dmf, biological studies
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonaq. polar aprotic peptide formulations)

L37 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1998:55544 HCAPLUS
DOCUMENT NUMBER:	128:132416
TITLE:	Aqueous formulations of peptides
INVENTOR(S):	Eckenhoff, James B.; Tao, Sally A.; Prestrelski, Steven J.; Wright, Jeremy C.; Leonard, Joe
PATENT ASSIGNEE(S):	Alza Corp., USA; Eckenhoff, Bonnie, J.; Stevenson, Cynthia L.; Tao, Sally A.; Prestrelski, Steven J.; Wright, Jeremy C.; Leonard, Joe
SOURCE:	PCT Int. Appl., 44 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800157	A1	19980108	WO 1997-US10816	19970701
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2259505	AA	19980108	CA 1997-2259505	19970701
AU 9735748	A1	19980121	AU 1997-35748	19970701
EP 909177	A1	19990421	EP 1997-932237	19970701

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

CN 1224357	A	19990728	CN 1997-196052	19970701
BR 9710131	A	19990810	BR 1997-10131	19970701
NO 9806208	A	19981230	NO 1998-6208	19981230
PRIORITY APPLN. INFO.:			US 1996-21199	19960703
			WO 1997-US10816	19970701

AB This invention relates to stable liq. aq. formulations of peptide compds. at high concns. These stable formulations comprise at least about 10 % peptide in water. They may be stored at elevated temps. for long periods of time and are esp. useful in implantable delivery devices for long term delivery of drug. Examples are given for stability testing of peptides such as leuprolide acetate in aq. formulations.

IC ICM A61K038-04
ICS A61K038-08; A61K038-09; A61K038-24; A61K047-08; A61K047-16; A61K047-18; A61K047-20; A61K047-02

CC **63-6** (Pharmaceuticals)

IT **Aprotic solvents**
Implants (drug delivery systems)
Parenteral solutions (drug delivery systems)
Preservatives
Solubilizers
(aq. formulations of peptides)

IT **67-68-5**, Dmso, biological studies 68-12-2, Dmf, biological studies
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(aq. formulations of peptides)

L37 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1996:701653 HCAPLUS
DOCUMENT NUMBER:	125:339040
TITLE:	Nanospheres comprising a biocompatible polysaccharide
INVENTOR(S):	Pallado, Paolo; Benedetti, Luca; Callegaro, Lanfranco
PATENT ASSIGNEE(S):	Fidia Advanced Biopolymers S.R.L., Italy
SOURCE:	PCT Int. Appl., 46 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9629998	A1	19961003	WO 1996-EP1354	19960326

W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2216919	AA	19961003	CA 1996-2216919	19960326
AU 9652749	A1	19961016	AU 1996-52749	19960326
AU 695207	B2	19980806		
EP 817620	A1	19980114	EP 1996-909138	19960326

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.:	IT 1995-PD65	19950328
	IT 1996-PD21	19960205
	WO 1996-EP1354	19960326

AB Microspheres, having a size lower than 1 .mu. and comprising a biocompatible polysaccharide polymer, are prepd. with a process comprising the pptn. of polymer induced by means of a supercrit. antisolvent (SAS). These microspheres are used as vehicle agents or carries in the prepn. of pharmaceutical compns. administrable by oral, nasal, pulmonary, vaginal or rectal route. These microspheres can also be advantageously used as vehicle agent or carriers in the prepn. of pharmaceutical compns. for the treatment of human diseases assocd. with genic defects, for the prepn. of diagnostics and in the agro-alimentary industry. Microspheres were prepd. according to the above procedure by dissolving Et hyaluronate in DMSO at a concn. of 0.1% followed by addn. of calcitonin at a concn. of 15 IU/mg of the polymer.

IC ICM A61K009-51

CC **63-6** (Pharmaceuticals)

ST **pharmaceutical** nanosphere biocompatible polysaccharide supercrit antisolvent; hyaluronate calcitonin **pharmaceutical** microsphere

IT **Solvents**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**aprotic**, nanospheres comprising biocompatible polysaccharide)

IT **Pharmaceutical** dosage forms
(inhalants, nanospheres comprising biocompatible polysaccharide)

IT **Pharmaceutical** dosage forms
(microspheres, nanospheres comprising biocompatible polysaccharide)

IT **Pharmaceutical** dosage forms
(nanospheres, nanospheres comprising biocompatible polysaccharide)

IT **Pharmaceutical** dosage forms
(nasal, nanospheres comprising biocompatible polysaccharide)

IT **Pharmaceutical** dosage forms
(oral, nanospheres comprising biocompatible polysaccharide)

IT **Pharmaceutical** dosage forms
(rectal, nanospheres comprising biocompatible polysaccharide)

IT **Pharmaceutical** dosage forms
(vaginal, nanospheres comprising biocompatible polysaccharide)

IT **67-68-5, Dimethyl sulfoxide**, biological studies 124-38-9, Carbon dioxide, biological studies 872-50-4, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(nanospheres comprising biocompatible polysaccharide)

L37 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:546570 HCAPLUS
DOCUMENT NUMBER: 125:257179
TITLE: Preparation of liposome and lipid complex compositions
INVENTOR(S): Szoka, Francis C. Jr.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S., 19 pp. Cont.-in-part of U.S. 5,277,791.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5549910	A	19960827	US 1994-179291	19940110
US 5077057	A	19911231	US 1990-605155	19901029
US 5277914	A	19940111	US 1991-741937	19910808
US 5567434	A	19961022	US 1995-480227	19950607
PRIORITY APPLN. INFO.:			US 1989-332609	19890331
			US 1989-334055	19890405
			US 1990-605155	19901029
			US 1991-741937	19910808
			US 1994-179291	19940110

AB Liposome and lipidic particle formulations of compds. are prepd. by dissolving a soln. of liposome-forming lipids in an aprotic solvent such as DMSO, optionally contg. a lipid-solubilizing amt. of a lower alkanol, and either injecting the resulting soln. into an aq. soln., or the aq. soln. into the resulting soln. The resulting liposome or lipidic particle suspension may then be dialyzed or otherwise concd. This method is particularly useful for compds. which are poorly-sol. in aq. soln., but is generally useful for any compd. or combination of compds. which can be dissolved in the aprotic solvent or aprotic solvent/lower alkanol mixt. Doxorubicin (I) was dissolved in DMSO and added to an ethanol soln. of egg phosphatidylglycerol, egg phosphatidylcholine, and cholesterol (7:3:6) to yield a final I concn. of 6.2 mM and a final total lipid concn. of 96.4 mM in DMSO:EtOH (7:3) solvent mixt. Lipid vesicles were formed by injecting 1 mL of the above mixt. into 2 mL of an aq. phase consisting of 140 mM NaCl, 10 mM Tris-HCl, pH 4.0, at 30.degree.. The lipid suspension was dialyzed against Tris buffer and the liposome-encapsulated I was sepd. from the nonencapsulated material by column chromatog. The resulting vesicle diam. was 227 nM and 41.2 % of the I was encapsulated in the vesicles.

IC ICM A61K009-127
ICS A61K051-02; B01J013-02; B01J013-20
NCL 424450000
CC **63-6** (Pharmaceuticals)
ST liposome lipid **aprotic solvent** drug encapsulation; doxorubicin phosphatidylcholine phosphatidylglycerol cholesterol DMSO encapsulation
IT **Pharmaceutical** dosage forms

(liposomes, **aprotic solvents** and lipids in prepn.
of liposomes and lipid complex compns.)
IT 64-17-5, Ethanol, biological studies 67-56-1, Methanol, biological studies **67-68-5, Dimethylsulfoxide**, biological studies 68-12-2, Dimethylformamide, biological studies 75-05-8, Acetonitrile, biological studies 96-48-0, .gamma.-Butyrolactone 120-94-5 123-91-1,
Dioxane, biological studies 126-33-0, Sulfolane **127-19-5**, **Dimethylacetamide** 872-50-4, 1-Methyl-2-pyrrolidinone, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as **aprotic solvent**; prepn. of liposomes and lipid complex compns.)

L37 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:498736 HCAPLUS
DOCUMENT NUMBER: 122:248269
TITLE: Estimation of some drugs capable of hydrogen bonding solubilities in dipolar **aprotic solvents**
AUTHOR(S): Martin, A.R.; Escalera Izquierdo, B.; Fresno Contreras, M.J.; Jimenez Duran, M.; Selles Flores, E.
CORPORATE SOURCE: Facultad de Farmacia, Universidad de Alcala de Henares, Madrid, Spain
SOURCE: Boll. Chim. Farm. (1994), 133(7), 473-5
CODEN: BCFAAI; ISSN: 0006-6648
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The soly. of two different classes of hydrogen bonding drugs, benzoic acid and their derivs. and sulfonamides, in dipolar aprotic solvents is studied theor. and empirically. The actual reported soly. in these solvents was higher than the ideal soly. and the difference could be expressed by a logarithm for the solute residual activity (ln .alpha.2R) which represents the acid-base Lewis interactions. The relation between the coeff. for the solute residual activity and the hydrogen bonding partial molar heat (.DELTA.H2h) is linear. This suggests that the hydrogen bonding heat could be calcd. with a substituent method like one suggested by Drago, or else with an exptl. calorimetric method.
CC **63-8** (Pharmaceuticals)
ST drug soly **aprotic solvent** hydrogen bonding
IT Hydrogen bond
Pharmaceuticals
Solubility
Solvent effect
(estn. of soly. of drugs capable of hydrogen bonding in dipolar **aprotic solvents**)
IT Sulfonamides
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estn. of soly. of drugs capable of hydrogen bonding in dipolar **aprotic solvents**)
IT 65-85-0, Benzoic acid, biological studies 67-64-1, Acetone, biological

studies **67-68-5, Dimethylsulfoxide**, biological studies
68-12-2, N,N-Dimethylformamide, biological studies 68-35-9, Sulfadiazine
80-35-3, Sulfamethoxypyridazine 99-76-3, Methyl p-hydroxybenzoate
99-96-7, p-Hydroxybenzoic acid, biological studies 123-39-7, N-Methylformamide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(estn. of soly. of drugs capable of hydrogen bonding in dipolar **aprotic solvents**)

L37 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:144177 HCAPLUS
DOCUMENT NUMBER: 120:144177
TITLE: **Pharmaceutical** liposome manufacture from compounds which are poorly soluble in aqueous solutions
INVENTOR(S): Szoka, Francis C., Jr.
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: U.S., 19 pp. Cont.-in-part of U.S. 5,077,057.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5277914	A	19940111	US 1991-741937	19910808
US 5077057	A	19911231	US 1990-605155	19901029
US 5549910	A	19960827	US 1994-179291	19940110
US 5567434	A	19961022	US 1995-480227	19950607
PRIORITY APPLN. INFO.:			US 1989-332609	19890331
			US 1989-334055	19890405
			US 1990-605155	19901029
			US 1991-741937	19910808
			US 1994-179291	19940110

AB Pharmaceutical liposome of compds. which are poorly sol. in aq. solns. are prepd. by dissolving the compd. and a liposome-forming lipid in an aprotic solvent such as DMSO, optionally contg. a lipid-solubilizing amt. of a lower alkanol, and either injecting the resulting soln. into an aq. soln., or the aq. soln. into the resulting soln. Amphotericin B (I) and chloresterol were dissolved in DMSO:EtOH 7:3 mixt. and the soln. was injected into a 10mM Hepes buffer pH=7.4 at 30.degree. to obtain liposomes having diam. of 451 nm which were dialyzed vs. distd. water. The above liposomes at 6-9 mg/kg/day were as effective as 4.5 mg/kg/day free I in immunosuppressed rabbits infected with Aspergillis fumioatus.
IC ICM A61K037-22
ICS A61K043-00; B01J013-02; B01J013-18
NCL 424450000
CC **63-6** (Pharmaceuticals)
ST **pharmaceutical** liposome poorly sol compd; amphotericin B DMSO

pharmaceutical liposome; **dimethylsulfoxide** amphotericin B **pharmaceutical** liposome

IT Phosphatidylglycerols
RL: BIOL (Biological study)
(egg yolk, **pharmaceutical** liposome manuf. with **aprotic solvents** and, of poorly sol. compds.)

IT Alcohols, biological studies
RL: BIOL (Biological study)
(**pharmaceutical** liposome manuf. with **aprotic solvents** and, of poorly sol. compds.)

IT Sulfonic acids, biological studies
RL: BIOL (Biological study)
(**pharmaceutical** liposome manuf. with, of poorly sol. compds.)

IT **Solvents**
(**aprotic, pharmaceutical** liposome manuf. with, of poorly sol. compds.)

IT Phosphatidylcholines, biological studies
RL: BIOL (Biological study)
(egg yolk, **pharmaceutical** liposome manuf. with **aprotic solvents** and, of poorly sol. compds.)

IT **Pharmaceutical** dosage forms
(liposomes, of poorly sol. compds., manuf. of, with **aprotic** org. **solvents**)

IT Phosphatidylcholines, biological studies
RL: BIOL (Biological study)
(soya, hydrogenated, **pharmaceutical** liposome manuf. with **aprotic solvents** and, of poorly sol. compds.)

IT 57-88-5, Cholesterol, biological studies 64-17-5, Ethanol, biological studies 1256-86-6, Cholesterol sulfate 1510-21-0, Cholesterol hemisuccinate 2644-64-6 4358-16-1, Cholesterol phosphate 13699-48-4,
Dimyristoylphosphatidylcholine 24951-79-9, Cholesterol phthalate 61361-72-6, Dimyristoylphosphatidylglycerol 65956-64-1, Cholesterylphosphocholine
RL: BIOL (Biological study)
(**pharmaceutical** liposome manuf. with **aprotic solvents** and, of poorly sol. compds.)

IT **67-68-5**, Dmso, biological studies 68-12-2, Dimethylformamide, biological studies 75-05-8, Acetonitrile, biological studies 96-48-0, Butyrolactone 123-91-1, Dioxane, biological studies **127-19-5, Dimethylacetamide** 554-15-4 872-50-4, 1-Methyl-2-pyrrolidinone, biological studies
RL: BIOL (Biological study)
(**pharmaceutical** liposome manuf. with, of poorly sol. compds.)

IT 51-43-4, Epinephrine 61-57-4, Niridazole 1397-89-3, Amphotericin b 1400-61-9, Nystatin 7681-93-8, Pimaricin 15663-27-1, Cisplatin 23214-92-8, Doxorubicin 31431-39-7, Mebendazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** liposomes contg., manuf. of, with **aprotic solvents**)

L37 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:567837 HCAPLUS
DOCUMENT NUMBER: 119:167837
TITLE: Microemulsions for gallstone dissolution
INVENTOR(S): Mayhan, Kenneth G.; Coulter, Stephen L.; Oviatt, Christy L. H.

PATENT ASSIGNEE(S): Baxter International Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9312774	A1	19930708	WO 1992-US10988	19921217

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1991-810994 19911220

AB Microemulsions, preferably oil-in-water, comprise org. component(s) having cholesterol soly. .gtoreq.2g/dL (25.degree.) and surfactant(s) are prepd. to dissolve gallstones. The org. components are alkyl esters or ethers, arom. hydrocarbons, terpenes, alkyl ketones, (poly)alcs., etc. The microemulsions, which are contacted with the gallstones via catheters, dissolve both cholesterol and noncholesterol gallstones. A microemulsion comprised Me tert-Bu ether 60, benzalkonium chloride 10, and water 30%. The microemulsions may also comprise mineral chelating agents and SS bond-cleaving agents.

IC ICM A61K031-08
ICS A61K009-107

CC **63-8** (Pharmaceuticals)

IT **Solvents**
(**aprotic**, dipolar, microemulsions contg., for gallstone dissoln.)

IT **Pharmaceutical** dosage forms
(microemulsions, for gallstone dissoln.)

IT 52-67-5, Penicillamine **56-81-5**, 1,2,3-Propanetriol, biological studies 59-52-9 60-00-4, EDTA, biological studies 60-29-7, Ethyl ether, biological studies 60-56-0 67-66-3, Chloroform, biological studies 71-41-0, Pentanol, biological studies 102-71-6, Triethanolamine, biological studies 107-15-3, 1,2-Ethanediamine, biological studies 108-88-3, Toluene, biological studies 110-80-5, 2-Ethoxyethanol 111-77-3, Diethyleneglycol monomethyl ether 112-00-5, Dodecyltrimethylammonium chloride 112-15-2, Diethyleneglycol monoethyl ether acetate 112-34-5, Diethyleneglycol monobutyl ether 123-03-5, Cetylpyridinium chloride 123-86-4, Butyl acetate 151-21-3, Sodium dodecyl sulfate, biological studies 151-67-7 616-91-1, N-Acetylcysteine 628-81-9, Ethyl butyl ether 1069-87-0 1119-94-4, Dodecyltrimethylammonium bromide 1330-20-7, Xylene, biological studies 1634-04-4, Methyl tert-butyl ether 2277-23-8 3483-12-3, Dithiothreitol 7758-29-4, Sodium tripolyphosphate 9002-93-1, Triton X-100 9002-98-6 12441-09-7D, Sorbitan, carboxylated 25155-30-0, Sodium dodecylbenzenesulfonate 25190-06-1 25265-75-2, Butylene glycol **25322-68-3** 25322-69-4 26402-26-6, Monooctanoin 150244-71-6
RL: USES (Uses)
(microemulsions contg., for gallstone dissoln.)

L37 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:175876 HCAPLUS
DOCUMENT NUMBER: 118:175876

TITLE: Vascular prosthesis
INVENTOR(S): Underwood, Christopher John; Charlesworth, David; Chian, Kerm Sin
PATENT ASSIGNEE(S): Newtec Vascular Products Ltd., UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9302636	A1	19930218	WO 1992-GB1337	19920721
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9223297	A1	19930302	AU 1992-23297	19920721
EP 596926	A1	19940518	EP 1992-915671	19920721
R: DE, FR, GB				
PRIORITY APPLN. INFO.:			GB 1991-16564	19910801
			WO 1992-GB1337	19920721

AB A vascular prosthesis comprises a flexible tube which accommodates pulsatile flow by increasing cross-sectional area by deformation of its cross-sectional shape. The prosthesis is made by coagulation casting onto a profiled mandrel a soln. of coagulatable polymer in an org. solvent. The polymer comprise polyurethaneurea, and the org. solvent is N,N-dimethylformaide.

IC ICM A61F002-06
ICS B29C047-00; B29C047-20; B29C067-06; A61L027-00

CC **63-7** (Pharmaceuticals)
Section cross-reference(s): 38

IT **Solvents**
(**aprotic**, vascular graft prepn. from coagulatable polymer and)

IT 68-12-2, n,n-Dimethylformamide, biological studies **127-19-5**, n,n-**Dimethylacetamide**
RL: BIOL (Biological study)
(vascular graft prepn. from coagulatable polymer and)

L37 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:175875 HCAPLUS
DOCUMENT NUMBER: 118:175875
TITLE: Vascular prosthesis
INVENTOR(S): Underwood, Christopher John
PATENT ASSIGNEE(S): Newtec Vascular Products Ltd., UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9302637 A1 19930218 WO 1992-GB1338 19920721
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG
AU 9223298 A1 19930302 AU 1992-23298 19920721
EP 596905 A1 19940518 EP 1992-914375 19920721
R: DE, FR, GB
PRIORITY APPLN. INFO.: GB 1991-16563 19910801
WO 1992-GB1338 19920721

AB A vascular prosthesis for use as access graft, e.g. in dialysis patients, is disclosed. The prosthesis has a permanent set, kink-resistant U-bend section. A soln. of coagulatable polymer, e.g. polyurethane, in an org. solvent, e.g. N,N-dimethylacetamide, was casted onto a mandrel to make the prosthesis (no data).

IC ICM A61F002-06
ICS B29C047-00; B29C047-20; B29C067-06; A61L027-00

CC **63-7** (Pharmaceuticals)
Section cross-reference(s): 38

IT **Solvents**
(**aprotic**, in prepn. of vascular prosthesis from coagulatable polymers)

IT Prosthetic materials and Prosthetics
(vascular, manuf. of, with coagulatable polymer and **aprotic solvent**)

IT 68-12-2, n,n-Dimethylformamide, biological studies **127-19-5**, n,n-**Dimethylacetamide**
RL: BIOL (Biological study)
(in prepn. of vascular prosthesis from coagulatable polymers)

L37 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:687172 HCAPLUS
DOCUMENT NUMBER: 115:287172
TITLE: Absorbent in podophyllotoxin purification process
INVENTOR(S): Jennings, Rex A.; Stearns, Jay F.
PATENT ASSIGNEE(S): Oclassen Pharmaceuticals, Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5057616	A	19911015	US 1989-415170	19890929

AB Podophyllotoxin (I) is recovered from podophyllum resin with improved efficiency by adsorbing impurities out of soln. using a solid adsorbent, esp. alumina. An overall process for I purifn. is described, including crystn., treatment with alumina, recrystn., and final vacuum dehydration.

IC ICM C07D307-77
NCL 549298000

CC **63-4** (Pharmaceuticals)
Section cross-reference(s): 11

IT **Solvents**
(co-, polar **aprotic**, in podophyllotoxin purifn. from

podophyllum resin)
IT 60-29-7, Diethyl ether, biological studies 64-17-5, Ethanol, biological studies **64-19-7**, Acetic acid, biological studies 71-43-2, Benzene, biological studies
RL: BIOL (Biological study)
(in podophyllotoxin purifn. from podophyllum resin)

L37 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:554301 HCAPLUS
DOCUMENT NUMBER: 111:154301
TITLE: Preparation of phosphatidylcholines for drugs, foods, and cosmetics
INVENTOR(S): Hibino, Hidehiko; Fukuda, Nobuo; Nakachi, Osamu
PATENT ASSIGNEE(S): Nippon Oils and Fats Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63225387	A2	19880920	JP 1987-56478	19870313

AB Title compds., useful for drugs, foods, and cosmetics (no data), are prepd. by treatment of 1 mol glycerophosphorylcholine (I) with 3.5-6 mol fatty acid anhydrides or halides in the presence of pyridines or tertiary amines as catalysts in aprotic high-polar solvents. Egg yolk lecithin (30 g) was treated with 80 mL MeOH soln. contg. 10% Bu4NOH in ether at room temp. for 10 min and left at room temp. for 2 h to give 6.1 g I. Treatment of 4.2 g palmitic acid with 1.6 g DCC in CCl4 at 40.degree. for 4 h gave 3.9 g palmitoyl anhydride which was treated with I and N,N-dimethyl-4-aminopyridine at 50.degree. in Me2SO for 4 h under vigorous stirring to afford 73% dipalmitoylphosphatidylcholine.
IC ICM C07F009-10
ICS B01J031-02
CC 33-6 (Carbohydrates)
Section cross-reference(s): 17, 62, **63**
ST phosphatidylcholine prepn drug food cosmetic; glycerophosphorylcholine acylation catalyst pyridine deriv; amine catalyst acylation glycerophosphorylcholine; **aprotic solvent** acylation glycerophosphorylcholine; fatty acid deriv acylation glycerophosphorylcholine
IT **Pharmaceuticals**
(heavy metal-free phosphatidylcholines as liposome for)
IT **Solvents**
(**aprotic**, high-polar, for acylation of glycerophosphorylcholine with fatty acid derivs.)
IT **67-68-5**, DMSO, uses and miscellaneous 68-12-2, DMF, uses and miscellaneous 680-31-9, HMPA, uses and miscellaneous
RL: USES (Uses)
(solvent, for acylation of glycerophosphorylcholine with fatty acid derivs.)

L37 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:75042 HCAPLUS
DOCUMENT NUMBER: 110:75042
TITLE: Process for preparing chlorinated diphenyl ethers, intermediates for **pharmaceuticals** and plant protective agents
INVENTOR(S): Rauber, Peter
PATENT ASSIGNEE(S): Ciba-Geigy Corp., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4766253	A	19880823	US 1987-46594	19870504
EP 297028	A2	19881228	EP 1988-810263	19880426
EP 297028	A3	19900523		
EP 297028	B1	19930818		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 93224	E	19930915	AT 1988-810263	19880426
ES 2058331	T3	19941101	ES 1988-810263	19880426
JP 63284141	A2	19881121	JP 1988-109850	19880502
JP 06086397	B4	19941102		
BR 8802145	A	19881206	BR 1988-2145	19880503
ZA 8803132	A	19881228	ZA 1988-3132	19880503
PRIORITY APPLN. INFO.:			US 1987-46594	19870504
			EP 1988-810263	19880426

OTHER SOURCE(S): MARPAT 110:75042

AB A process for prepg. ethers I (R = H, Cl) comprises heating RC6H4OX (X = 1 equiv. alkali metal or alk. earth metal ion) in an excess comprising 3-15 mol Cl2C6H4 in the presence of a Cu catalyst and 0.003-3 mol of an aprotic solvent as cocatalyst at 120-220.degree.. NaOH (50%) was added to 4-ClC6H4OH, 1,3-Cl2C6H4, and AcNMe2, the mixt. heated to 150.degree., and CuO added to give 80% 4-(3-ClC6H4O)C6H4Cl (II).

IC ICM C07C041-16
ICS C07C043-275; C07C043-29
NCL 568639000
CC 25-10 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 5
ST chlorinated diphenyl ether intermediate; chlorodiphenyl ether intermediate; **pharmaceutical** intermediate chlorodiphenyl ether prepn; plant protectant intermediate chlorodiphenyl ether prepn; phenyl ether chloro intermediate
IT **Pharmaceuticals**
(intermediates for, chlorinated di-Ph ethers as)
IT 7440-50-8, Copper, uses and miscellaneous 7447-39-4, Cupric chloride, uses and miscellaneous 7681-65-4, Cuprous iodide 7758-89-6, Cuprous chloride 7758-98-7, Cupric sulfate, uses and miscellaneous 7787-70-4, Cuprous bromide 7789-45-9, Cupric bromide 20427-59-2, Cupric hydroxide
RL: USES (Uses)
(**aprotic** dipolar **solvent** as cocatalyst and, as catalyst for reaction of alkali metal or alk. earth metal

chlorophenolate and dichlorophenol)
IT 544-92-3, Cuprous cyanide 598-54-9, Cuprous acetate 1184-64-1
1317-38-0, Cupric oxide, uses and miscellaneous 1317-39-1, Cuprous oxide, uses and miscellaneous 3251-23-8, Cupric nitrate
RL: RCT (Reactant)
(**aprotic** dipolar **solvent** as cocatalyst and, as catalyst for reaction of alkali metal or alk. earth metal chlorophenolate and dichlorophenol)
IT 62-53-3, Benzenamine, uses and miscellaneous **67-68-5**, uses and miscellaneous 68-12-2, Dimethylformamide, uses and miscellaneous 75-05-8, Acetonitrile, uses and miscellaneous 75-12-7, Formamide, uses and miscellaneous 680-31-9, Hexamethylphosphoramide, uses and miscellaneous 872-50-4, uses and miscellaneous
RL: USES (Uses)
(cocatalysts with copper or compd., for reaction of sodium chlorophenolates with dichlorobenzenes)
IT 96-49-1, Ethylene carbonate 100-47-0, Benzonitrile, uses and miscellaneous 100-61-8, Methylaniline, uses and miscellaneous 107-12-0, Propanenitrile 108-32-7, Propylene carbonate 109-74-0, Butyronitrile 110-71-4, 1,2-Dimethoxyethane 110-86-1, Pyridine, uses and miscellaneous 111-92-2, Dibutylamine 111-96-6 121-69-7, Dimethylaniline, uses and miscellaneous 123-39-7, N-Methylformamide **127-19-5**
RL: RCT (Reactant)
(cocatalysts with copper or compd., for reaction of sodium chlorophenolates with dichlorobenzenes)
IT 6842-62-2P, 3,4'-Dichlorodiphenyl ether 6903-65-7P, 2,4'-Dichlorodiphenyl ether
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for **pharmaceuticals** and plant protective agents)

L37 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:642674 HCAPLUS
DOCUMENT NUMBER: 107:242674
TITLE: Polymeric microporous membranes for the electronic and **pharmaceutical** industries and their manufacture
INVENTOR(S): Kraus, Menahem A.; Heisler, Mark D.; Katsnelson, Inessa Nmi; Velazquez, Diosie J.
PATENT ASSIGNEE(S): Gelman Sciences, Inc., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 228072	A2	19870708	EP 1986-117950	19861223
EP 228072	A3	19890705		
EP 228072	B1	19910828		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 8666949	A1	19870625	AU 1986-66949	19861223
AU 593866	B2	19900222		

JP 62258707	A2	19871111	JP 1986-307552	19861223
JP 05076331	B4	19931022		
IL 81082	A1	19900712	IL 1986-81082	19861223
AT 66633	E	19910915	AT 1986-117950	19861223
CA 1320024	A1	19930713	CA 1986-526221	19861223
JP 10225629	A2	19980825	JP 1997-55327	19970310
JP 3060985	B2	20000710		
PRIORITY APPLN. INFO.:			US 1985-812260	19851223
			US 1985-812343	19851223
			US 1986-897045	19860815
			EP 1986-117950	19861223
			JP 1986-307552	19861223

AB Microporous filtration membranes, useful for the prepn. of particle- and bacteria-free water or solns. for the electronic and pharmaceutical industries, comprise a hydrophobic polymer in bulk form having a sp. water absorption and pore size and a high water flow rate at any given bubble point, and an additive polymer. The membrane is hydrophilic in polymd. form or when contg. 1-6 wt.% additive polymer. Polyether sulfone (Victorex 5200), DMF, and polyethylene glycol 400 were mixed in 13:69 ratio, stir-cast at 10-12 mil on glass, opacified in ambient air and 60-70% relative humidity, coagulated in H2O, and dried at 70.degree. to give a spontaneously wettable membrane showing water bubble point 53 lbs/in2, air flow 2.7 L/cm2-min at 10 lbs/in2, and water flow 23 mL/cm2-min at 10 lbs/in2. The membrane exhibited 100% bacteria retention in the presence of 107 Pseudomonas dimunitae/cm2.

IC ICM B01D013-04
ICS C08J003-08; C08L081-06; C08L079-08

CC **63-8** (Pharmaceuticals)
Section cross-reference(s): 30, 76

IT 9003-39-8, Polyvinylpyrrolidone **25322-68-3, Polyethylene glycol**
RL: DEV (Device component use); USES (Uses)
(membranes contg., microporous, for bacteria and particle removal)

IT 51013-18-4, Methylpyrrolidone 68-12-2, Dimethylformamide, uses and miscellaneous **127-19-5, Dimethylacetamide**
RL: BIOL (Biological study)
(**solvent, aprotic,** for microporous membrane manuf.)

L37 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1984:91416 HCAPLUS
DOCUMENT NUMBER: 100:91416
TITLE: Insulin formulations
INVENTOR(S): McMullen, John Kenneth
PATENT ASSIGNEE(S): UK
SOURCE: Brit. UK Pat. Appl., 7 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2119248	A1	19831116	GB 1983-11420	19830427
PRIORITY APPLN. INFO.:			GB 1982-12221	19820428

AB An insulin [9004-10-8] formulation comprises a soln. of the hormone in a

dipolar aprotic solvent. A method of purifying insulin includes introducing a soln. of impure insulin in a dipolar aprotic solvent into deionized water and then removing the pptd. insulin. Thus, insulin crystals were dissolved in the solvents such as DMSO [**67-68-5**], 5,5-dimethyl-1,3-cyclohexanedione [126-81-8], or dimethyl sulfolane [26445-81-8]. The formulations are stable, noncorrosive, and are esp. suitable for use in implanted pump delivery systems.

IC A61K037-26
CC **63-6** (Pharmaceuticals)
ST insulin formulation **aprotic solvent**; DMSO insulin formulation; cyclohexanedione insulin formulation; sulfolane insulin formulation; pump delivery insulin
IT **Solvents**
(**aprotic**, insulin formulations in, for implanted pump delivery system)
IT 9004-10-8, biological studies
RL: BIOL (Biological study)
(formulations, in **aprotic solvents**, for implanted pump delivery system)
IT **67-68-5**, biological studies 126-81-8 26445-81-8
RL: BIOL (Biological study)
(insulin formulations in, for implanted pump delivery system)

L37 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1983:443378 HCAPLUS
DOCUMENT NUMBER: 99:43378
TITLE: Phenindione solubility in mixed organic solvents: analysis of the role of specific hydrogen and nonhydrogen bonding interactions
AUTHOR(S): Pipkin, J. D.; Stella, V. J.
CORPORATE SOURCE: Dep. Pharm. Chem., Univ. Kansas, Lawrence, KS, 66045, USA
SOURCE: Int. J. Pharm. (1983), 14(2-3), 263-77
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Phenindione (I) [83-12-5] exists predominantly in its diketo rather than its enol form in hydrocarbon solvents. Basic mols. interact with I in cyclohexane [110-82-7] resulting in the formation of a tautomeric enol-complex. The soly. of hydrogen bond donor mols. in the presence of bases can often be defined by specific chem. or hydrogen bond interactions. The soly. of I in cyclohexane in the presence of increasing concns. of a no. of dipolar bases, cosolvents, was studied. In the presence of strong bases, the soly. was predicted well by the increased of the enol-complex; however, in the presence of weak bases, the nonspecific chem. and/or phys. effects were also operative.

CC **63-5** (Pharmaceuticals)
Section cross-reference(s): 22
ST phenindione soly **solvent**; hydrogen bonding phenindone soly; enolization phenindione **aprotic solvent**
IT Tautomerization
(enolization, of phenindione, in cyclohexane contg. dipolar **aprotic solvents**, soly. in relation to)
IT **67-68-5**, properties 68-12-2, properties 108-94-1, properties 110-86-1, properties 115-86-6 **127-19-5** 632-22-4

RL: PRP (Properties)
(phenindione soly. in cyclohexane contg., hydrogen and nonhydrogen bonding interactions in)
IT 110-82-7, properties
RL: PRP (Properties)
(phenindione soly. in mixts. of dipolar **aprotic solvent** and, hydrogen and nonhydrogen bonding interactions in)
IT 83-12-5
RL: PRP (Properties)
(soly. of, in cyclohexane contg. dipolar **aprotic solvents**, hydrogen and nonhydrogen bonding interactions in)

L37 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1982:53079 HCAPLUS
DOCUMENT NUMBER: 96:53079
TITLE: Molecular structure of solutions of aromatic polyamides in **aprotic solvents** with **lyophilic** salts
AUTHOR(S): Mitchenko, Yu. I.; Tsiperman, R. F.; Lebedeva, T. I.
CORPORATE SOURCE: USSR
SOURCE: 3-i Mezhdunar. Simpoz. po Khim. Voloknam, Kalinin, 1981, Kalinin (1981), (1), 292-301
From: Ref. Zh., Khim. 1981, Abstr. No. 22S78
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Title only translated.
CC 36-7 (Physical Properties of Synthetic High Polymers)
ST polyamide structure soln salt; **lyophilic** salt polyamide soln
IT Polyamides, properties
RL: PRP (Properties)
(arom., interaction of, with **aprotic solvents** contg. **lyophilic** salts)
IT 7447-41-8, uses and miscellaneous 10043-52-4, uses and miscellaneous
RL: USES (Uses)
(**aprotic solvents** contg., polyamide interaction with)
IT 24938-60-1 25035-33-0
RL: PRP (Properties)
(interaction of, with **aprotic solvents** contg. **lyophilic** salts)
IT **127-19-5** 680-31-9, properties 872-50-4, properties
RL: PRP (Properties)
(polyamide interaction with **lyophilic** salt-contg.)

L37 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1980:82442 HCAPLUS
DOCUMENT NUMBER: 92:82442
TITLE: Stable solutions of PGE-type compounds
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: Israeli, 21 pp.
CODEN: ISXXAQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

IL 44740	A1	19780615	IL 1974-44740	19740430
IL 40517	A1	19750313	IL 1972-40517	19721006
ZA 7402960	A	19750827	ZA 1974-2960	19740509
GB 1457327	A	19761201	GB 1974-20837	19740510
PRIORITY APPLN. INFO.:			IL 1972-40517	19721006
			US 1973-359846	19730511
			US 1971-194686	19711101
			US 1973-359486	19730511

AB Prostaglandins are stabilized by dissolving in an anhyd. H2O-miscible, pharmacol. acceptable, dipolar aprotic solvent. Thus, PGE1 [745-65-3] was dissolved in anhyd. Me2NAc [**127-19-5**] (contg. 0.4% H2O) in proportions of 5 mg PGE1/mL Me2NAc. The soln. was filter sterilized and packaged in 1 mL quantities in ampuls. One ampul can be dild. into 1 L infusion soln. for i.v. administration at 5 .mu.g PGE1/min as an abortifacient.

CC **63-6** (Pharmaceuticals)

IT Prostaglandins
RL: BIOL (Biological study)
(solns., stabilization of, water-miscible dipolar **aprotic solvents** for)

IT 745-65-3
RL: PROC (Process)
(in soln., stabilization of, **dimethylacetamide** solvent for)

IT **127-19-5**
RL: BIOL (Biological study)
(prostaglandin soln. stabilization by)

L60 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	2000:566351 HCAPLUS
DOCUMENT NUMBER:	133:292932
TITLE:	Photophysical consequences of coupling bacteriochlorophyll a with serine and its resulting solubility in water
AUTHOR(S):	Eichwurzel, I.; Stiel, H.; Teuchner, K.; Leupold, D.; Scheer, H.; Salomon, Y.; Scherz, A.
CORPORATE SOURCE:	Max-Born-Institut fuer Nichtlineare Optik und Kurzzeitspektroskopie, Berlin, D-12489, Germany
SOURCE:	Photochem. Photobiol. (2000), 72(2), 204-209 CODEN: PHCBAP; ISSN: 0031-8655
PUBLISHER:	American Society for Photobiology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The authors investigated the dependence on solvents of optical absorption and emission of the bacteriochlorophyll a-serine (BChl-ser), a water-sol. bacteriochlorophyll (BChl) deriv. Comparison between the exptl. data and those collected for BChl in nonaq. solvents shows that only a minor interaction takes place between serine and the macrocycle's .pi.-electron system. Nevertheless, the coupling with serine results in a small enhancement of the nonradiative relaxation rate from the first excited singlet state S1. In buffered aq. soln. (pH = 7.4), the Stokes shift of the BChl-ser fluorescence and its nonradiative relaxation rate are enhanced compared with those in nonaq. solns. (Scherz, A. et al., 1998), probably as a result of a hydrogen bonding between the BChl macrocycle and

the water mols. In **aprotic** solvents, without hydrogen bonds, the permanent dipole moment of the first excited singlet state in both BChl and BChl-ser is increased compared with the ground state by at least 2.5 Debye.

CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 11, 26, 34, 73

IT Photosensitizers (**pharmaceutical**)
(solvent effect on absorption and fluorescence of bacteriochlorophyll a coupled with serine as)

IT 60-29-7, Diethyl ether, properties 64-17-5, Ethanol, properties 67-56-1, Methanol, properties 67-64-1, Acetone, properties 67-66-3, Chloroform, properties **67-68-5**, DMSO, properties 78-83-1, Isobutanol, properties 7732-18-5, Water, properties
RL: PRP (Properties)
(**solvent** effect on photophys. properties of bacteriochlorophyll a coupled with serine)

REFERENCE COUNT: 30
REFERENCE(S):
(1) Abdel-Halim, S; J Chem Soc Faraday Trans 1993, V89, P55 HCAPLUS
(2) Alden, R; J Phys Chem B 1997, V101, P4667 HCAPLUS
(3) Brereton, R; J Chem Soc Perkin Trans 1 1983, P431 HCAPLUS
(4) Connolly, J; Photochem Photobiol 1982, V36, P565 HCAPLUS
(6) Evans, T; Biochim Biophys Acta 1975, V396, P414 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:709054 HCAPLUS
DOCUMENT NUMBER: 129:330662
TITLE: Process for producing quinolone derivatives
INVENTOR(S): Osawa, Tatsushi; Kubo, Kazuo; Murooka, Hideko; Nakajima, Tatsuo
PATENT ASSIGNEE(S): Kirin Beer Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9847873	A1	19981029	WO 1998-JP1708	19980415
W: CN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 990647	A1	20000405	EP 1998-914017	19980415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6187926	B1	20010213	US 1999-420521	19991018
PRIORITY APPLN. INFO.:			JP 1997-101220	19970418
			WO 1998-JP1708	19980415

OTHER SOURCE(S): CASREACT 129:330662; MARPAT 129:330662
AB This document discloses a process for producing 4-quinolone derivs. I [A,

B, C, D = H, alkyl, etc.] by reacting an o-aminoacetophenone deriv. with a formic ester in the presence of a suitable base in an **aprotic** solvent and then adding a protonic solvent to the reaction mixt. I are intermediates for pharmaceuticals and agrochems. An industrial mass prodn. of 4-quinolone derivs. can be done by this process. Thus, a mixt. of 6-amino-3,4-(methylenedioxy)acetophenone 5 g and sodium methoxide 4.5 g in dimethoxyethane 150 mL 100 mL was stirred at room temp. for 30 min; Et formate 12 mL was added to the reaction mixt., and the resulting mixt. was stirred at room temp. for 160 min; water 5 mL was then added to the reaction mixt. which was stirred for a further 10 min to give, after workup and purifn., 6,7-(methylenedioxy)-4-quinolone in 94% yield.

IC ICM C07D215-22
ICS C07D491-056

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 5

ST quinolone prepn **pharmaceutical** agrochem intermediate; cyclocondensation aminoacetophenone ethyl formate

IT 64-17-5, Ethanol, uses **64-19-7**, Acetic acid, uses 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses 68-12-2, DMF, uses 71-43-2, Benzene, uses 75-05-8, Acetonitrile, uses 108-88-3, Toluene, uses 108-90-7, Chlorobenzene, uses 109-99-9, THF, uses 110-71-4 123-91-1, Dioxane, uses 7732-18-5, Water, uses 62309-51-7, Propanol
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(**solvent**; process for producing quinolone derivs.)

L60 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:732997 HCAPLUS
DOCUMENT NUMBER: 127:318880
TITLE: Process for producing 2-alkylchroman-6-carbonitriles
INVENTOR(S): Eszenyi, Tibor; Timar, Tibor; Csaki, Erika; Fazekas, Lajosne; Seboek, Peter; Istvan, Zoltanne
PATENT ASSIGNEE(S): Icn Alkaloida Magyarorszag Reszvenytarsasag, Hung.
SOURCE: Hung. Teljes, 29 pp.
CODEN: HUXXBU
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 75699	A2	19970528	HU 1995-2098	19950710

OTHER SOURCE(S): MARPAT 127:318880

AB 2-Alkylchroman-6-carbonitriles I (R2 = H, C1-4-alkoxy or -aralkoxy, R3 = H, R4 = C1-4-alkyl) were prepd. by: (a) redn. of ketones II (R1 = H, R' = C1-4 alkyl) in a dipolar protic solvent with a complex metal hydride at 0-100.degree. (preferably in MeOH with NaBH4 at 25-50.degree.) to carbinols III (R3 = H, R4 = C1-4-alkyl); (b) cyclodehydration of the latter in a water-immiscible azeotrope-forming org. solvent in presence of mineral or org. acid at 0-100.degree. (preferably in benzene in presence of p-TsOH at 70-80.degree.) to chromans IV (R1 = H, R2 = H, C1-4-alkoxy or

-aralkoxy, R3 = H, R4 = C1-4-alkyl); (c) regioselective bromination of the latter with Br2 in a halogenated hydrocarbon solvent at -20.degree. to 100.degree. (preferably in CCl4 at 0-5.degree.) to 6-bromochroman V; and (d) cyanation of the latter with with CuCN in a dipolar **aprotic** solvent at 50-200.degree. (preferably in N-methyl-2-pyrrolidone at 160-200.degree.) to provide I. Thus, e.g., redn. of 4-(2'-hydroxyphenyl)-2-butanone with NaBH4 followed by p-TsOH treatment afforded 60% 2-methylchroman.

IC ICM C07D311-22
CC 27-14 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): **63**
IT 56-23-5, Carbon tetrachloride, uses 60-29-7, Diethyl ether, uses 64-17-5, Ethanol, uses **64-19-7**, Acetic acid, uses 67-56-1, Methanol, uses 67-66-3, Chloroform, uses 71-43-2, Benzene, uses 108-24-7, Acetic anhydride 872-50-4, N-Methyl-2-pyrrolidone, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(**solvent**; process for producing 2-alkylchroman-6-carbonitriles)

L60 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:540685 HCAPLUS
DOCUMENT NUMBER: 125:196061
TITLE: Preparation of tocopheryl ascorbyl phosphates as **pharmaceuticals**
INVENTOR(S): Nakamura, Masayuki
PATENT ASSIGNEE(S): Senju Pharma Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08157488	A2	19960618	JP 1994-301918	19941206

OTHER SOURCE(S): CASREACT 125:196061
AB The title compds. I, II, or their salts, useful for treatment of cataract, circulatory disease, menopausal disorder, etc. (no data), are prepd. by reaction of tocopherol halophosphates with ascorbic acid in **aprotic** polar solvents in the presence of dehydrohalogenation agents. Ascorbic acid was treated with dl-.alpha.-tocopherol phosphorodichloridate in DMSO-THF in presence of K2CO3 at 0-10.degree. for 4.5 h to give 28% I mono-K salt.
IC ICM C07F009-6558
ICA A61K031-665
CC 30-20 (Terpenes and Terpenoids)
Section cross-reference(s): 33
ST tocopheryl ascorbyl phosphate prepn **pharmaceutical**; esterification ascorbate phosphate solvent
IT 554-13-2, Lithium carbonate 584-08-7, Potassium carbonate
RL: RCT (Reactant)
(dehydrohalogenation agent; prepn. of tocopheryl ascorbyl phosphates as

pharmaceuticals)
IT 96301-17-6P 132697-38-2P 180639-36-5P 180639-37-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of tocopheryl ascorbyl phosphates as **pharmaceuticals**)
IT 50-81-7, Ascorbic acid, reactions 107242-61-5
RL: RCT (Reactant)
(prepn. of tocopheryl ascorbyl phosphates as **pharmaceuticals**)
IT **67-68-5, Dimethyl sulfoxide,** uses 80-73-9, 1,3-Dimethyl-2-imidazolidinone 109-99-9, Thf, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(**solvent;** prepn. of tocopheryl ascorbyl phosphates as **pharmaceuticals**)

L60 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:319142 HCAPLUS
DOCUMENT NUMBER: 125:58087
TITLE: Process for the preparation of optically pure (+)-2-(3,4-dichlorophenyl)-4-hydroxybutylamine
INVENTOR(S): Descamps, Marcel; Radisson, Joel; Anne-archard, Gilles
PATENT ASSIGNEE(S): Sanofi, Fr.
SOURCE: U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 202,027, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5512680	A	19960430	US 1994-294035	19940824
FR 2701946	A1	19940902	FR 1993-2262	19930226
FR 2701946	B1	19950524		
IL 114866	A1	19991222	IL 1995-114866	19950808
ZA 9507025	A	19960326	ZA 1995-7025	19950822
CA 2156764	AA	19960225	CA 1995-2156764	19950823
NO 9503313	A	19960226	NO 1995-3313	19950823
EP 698601	A1	19960228	EP 1995-401935	19950823
EP 698601	B1	19981104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AU 9530216	A1	19960307	AU 1995-30216	19950823
AU 685971	B2	19980129		
BR 9503776	A	19960416	BR 1995-3776	19950823
RU 2097376	C1	19971127	RU 1995-114391	19950823
AT 172964	E	19981115	AT 1995-401935	19950823
ES 2125574	T3	19990301	ES 1995-401935	19950823
FI 9503994	A	19960225	FI 1995-3994	19950824
JP 08176108	A2	19960709	JP 1995-216328	19950824
JP 3037592	B2	20000424		
HU 74184	A2	19961128	HU 1995-2481	19950824
US 5780666	A	19980714	US 1996-598001	19960207
PRIORITY APPLN. INFO.:			FR 1993-2262	19930226
			US 1994-202027	19940225
			US 1994-294035	19940824

OTHER SOURCE(S): CASREACT 125:58087; MARPAT 125:58087
AB A process is described for the prepn. of (+)-2-(3,4-dichlorophenyl)-4-hydroxybutylamine which comprises (a) treating 3,4-dichlorophenylacetonitrile with an alkali metal chloroacetate or bromoacetate in liq. ammonia or in a polar **aprotic** solvent, in the presence of a strong base, at a temp. of -40.degree. to +25.degree.; (b) treating the resulting racemic 3-cyano-3-(3,4-dichlorophenyl)propionic acid with D-(-)-N-methylglucamine in order to crystallize all the acid in the form of the D-(-)-N-methylglucamine salt of the levorotatory acid; (c) treating said salt with a strong acid; and (d) subjecting the freed (-)-3-cyano-3-(3,4-dichlorophenyl)propionic acid to enantioconservative redn. with a borane. A mixt. of 186 g (1.00 mol) of 3,4-dichlorophenylacetonitrile, 126 g (1.05 mol) of sodium chloroacetate and 105 g (1.05 mol) of NaOBu-tert is reacted for 4 h at -33.degree. in 1 L of liq. NH3; the conc. remaining after acidic workup is redissolved in 2 L of abs. EtOH, the soln. is heated and 292 g of D-(-)-N-methylglucamine are added; after crystn., the product is filtered off, rinsed with EtOH and dried under vacuum to give 396 g of the N-methylglucamine salt of (-)-3-cyano-3-(3,4-dichlorophenyl)propionic acid (91% yield based on 3,4-dichlorophenylacetonitrile); the free acid is obtained in 76.5% yield (based on 3,4-dichlorophenylacetonitrile) by treatment with HCl. Redn. of 244 g (1 mol) of (-)-3-cyano-3-(3,4-dichlorophenyl)propionic acid in 500 mL of THF at 0.degree. with 350 mL of a 1 M soln. of BH3 in THF afforded 68% (+)-2-(3,4-dichlorophenyl)-4-hydroxybutylamine.
IC ICM C07D211-58
ICS C07C253-30; C07C255-41; C07C213-00
NCL 546224000
CC 25-7 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): **63**
IT **67-68-5**, DMSO, uses 68-12-2, DMF, uses 7664-41-7, Ammonia, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(**solvent**; prepn. of optically pure (+)-2-(3,4-dichlorophenyl)-4-hydroxybutylamine)

L60 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:137926 HCAPLUS
DOCUMENT NUMBER: 124:317891
TITLE: Onium-induced lactamization of methionine analogs in preparation of amidinophenyl pyrrolidine .beta.-alanine urea analogs useful as antithrombotics
INVENTOR(S): Abood, Norman A.; Flynn, Daniel L.; Laneman, Scott A.; Nosal, Roger; Schretzman, Lori A.
PATENT ASSIGNEE(S): G. D. Searle and Co., USA
SOURCE: U.S., 13 pp. Division of U.S. Ser. No. 349,333.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5484946	A	19960116	US 1995-463657	19950605
US 5610296	A	19970311	US 1994-349333	19941205
US 5576447	A	19961119	US 1995-465212	19950605
US 5659063	A	19970819	US 1995-467417	19950606
CA 2207102	AA	19960613	CA 1995-2207102	19951204
WO 9617827	A1	19960613	WO 1995-US14948	19951204
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9641636	A1	19960626	AU 1996-41636	19951204
EP 796245	A1	19970924	EP 1995-940016	19951204
EP 796245	B1	20000726		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 10509960	T2	19980929	JP 1995-517599	19951204
AT 194976	E	20000815	AT 1995-940016	19951204
ES 2150592	T3	20001201	ES 1995-940016	19951204
PRIORITY APPLN. INFO.:			US 1994-349333	19941205
			WO 1995-US14948	19951204

OTHER SOURCE(S): CASREACT 124:317891; MARPAT 124:317891

AB A process is claimed for the prepn. of a lactam of the formula I wherein R is a protecting group selected from the group consisting of t-butoxycarbonyl and carbobenzyloxy, wherein Z is selected from the group consisting of CN, CONH2 and CO2-alkyl comprising: treating a methionine analog of the formula II with a compd. selected from trimethylsulfonium halide and trimethylsulfoxonium halide, in the presence of a base in an **aprotic** solvent. The invention herein is further directed to the prepn. of amidinophenyl pyrrolidinyl .beta.-alanine urea analogs using such methionine and lactam compds. as intermediates, which .beta.-alanine urea analogs are useful as antithrombotics (no data). Thus, e.g., to a soln. of L-BOC-methionine (100.0 g, 0.40 mol), 4-aminobenzamide (57.3 g, 0.42 mol) and CMPI (2-chloro-1-methylpyridinium iodide, 102.6 g, 0.40 mol) in 250 mL of DMF at 0.degree. under N2 was added NMM (N-methylmorpholine, 88 mL, 0.8 mol) over 2 min; workup afforded 84% N-[(4-aminocarbonyl)phenyl]-4-methylthio-2(S)-[[(1,1-dimethylethoxy)carbonyl]amino]butanamide (III). To a soln. of III (3.00 g, 8.16 mmol) in DMSO (6 mL) was added trimethylsulfonium iodide (5.00 g, 24.48 mmol) and powd. K2CO3 (1.69 g, 12.24 mmol); workup afforded 75% 1-[(4-aminocarbonyl)phenyl]-3(S)-[[(1,1-dimethylethoxy)carbonyl]amino]pyrrolidin-2-one (IV).

IC ICM C07D207-273
NCL 548543000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, **63**
IT **67-68-5**, DMSO, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(**solvent**; onium-induced lactamization of methionine analogs in prepn. of amidinophenyl pyrrolidine .beta.-alanine urea analogs useful as antithrombotics)

L60 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:532006 HCAPLUS
DOCUMENT NUMBER: 122:267455
TITLE: Membranes from acrylonitrile copolymers and their preparation and use
INVENTOR(S): Hildenbrand, Karlheinz; Dhein, Rolf; Ebert, Wolfgang; Hugl, Herbert; Engelhard, Helmut; Wilken, Hans Joachim
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger., 5 pp.
CODEN: GWXXAW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4325650	C1	19940922	DE 1993-4325650	19930730
EP 636404	A1	19950201	EP 1994-111140	19940718
EP 636404	B1	19980114		
R: BE, DE, ES, FR, GB, IE, IT, NL, PT, SE				
ES 2111214	T3	19980301	ES 1994-111140	19940718
JP 07060085	A2	19950307	JP 1994-192271	19940725
PRIORITY APPLN. INFO.:			DE 1993-4325650	19930730
			DE 1993-4341601	19931207

AB Asym. membranes comprising copolymers of 70-95% acrylonitrile and 5-30% other nonionic vinyl or (meth)acrylic monomers (esp. vinyl acetate) are prepd. by phase inversion using solvents selected from N-methylpyrrolidone or its mixts. with other polar **aprotic** solvents, DMF-AcNMe2 mixts., and DMSO-DMF mixts. with H2O as the pptn. agent. The membranes are useful for hemodialysis, hemodiafiltration, reverse osmosis, and nanofiltration.
IC ICM B01D071-42
ICS B01D067-00; A23C009-142; A61M001-28
ICA B01D069-04; B01D069-06; B01D069-08
CC 38-3 (Plastics Fabrication and Uses)
Section cross-reference(s): **63**
IT **67-68-5, Dimethyl sulfoxide**, uses 68-12-2, Dimethylformamide, uses **127-19-5, Dimethylacetamide** 872-50-4, N-Methylpyrrolidone, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(**solvents**; for prepn. of acrylonitrile copolymer membranes by phase inversion)

L60 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:569270 HCAPLUS
DOCUMENT NUMBER: 119:169270
TITLE: Process for producing electrically impervious anodized films on valve metals and product thereof
INVENTOR(S): Cooper, Mathew; Rosenberg, Harry
PATENT ASSIGNEE(S): Alta Group, USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5211832	A	19930518	US 1992-872061	19920422
CA 2091147	AA	19931023	CA 1993-2091147	19930305
JP 07268688	A2	19951017	JP 1993-75030	19930310
EP 569121	A1	19931110	EP 1993-301926	19930315
R: BE, DE, FR, GB, IT, NL				
PRIORITY APPLN. INFO.:			US 1992-872061	19920422

AB A method is described for producing an anodized film on Ti, its alloys, and other metals such that the film deposited will have a specific leak rate of <1 nA/cm2 at room temp. with an impressed elec. field of .gtoreq.5 V, where the anodization is performed in a soln. consisting of liq. H3PO4 of reduced water content in an **aprotic** solvent. Articles of manuf. therefrom include prosthetic devices and electrolytic capacitors.

IC ICM C25D011-08
ICS C25D011-26
NCL 205322000
CC 72-7 (Electrochemistry)
Section cross-reference(s): 56, **63**, 76
IT **67-68-5, Dimethyl sulfoxide**, uses 96-48-0, Butyrolactone 96-49-1, Ethylene carbonate 108-32-7, Propylene carbonate 126-33-0, Sulfolane 872-50-4, N-2-Methylpyrrolidone, uses 2687-91-4, N-2-Ethylpyrrolidone
RL: USES (Uses)
(**solvent**, in anodization of valve metals)

L60 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:228970 HCAPLUS
DOCUMENT NUMBER: 114:228970
TITLE: Method for purification of diltiazem hydrochloride
INVENTOR(S): Dejmek, Lubos; Strof, Jiri; Smrz, Rudolf
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 4 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 268354	B1	19900314	CS 1988-161	19880106

AB Crude title compd. (I.HCl; R = Ac) (II), was purified by crystn. from a dipolar **aprotic** solvent or a 2-solvent system comprising a crystn. solvent, e.g., an aliph. ester, alc., ether, or ketone, and a dipolar **aprotic** solvent, preferably an aliph. acid (N-alkyl) amide or (N-alkyl) lactam. Thus, a soln. of 1.0 kg crude II contg. 0.8% I (R = H) free base (III) and 1.4% III.HCl in 4.0 L DMF was treated with 60 g activated C at 100-110.degree. and filtered hot, the stirred filtrate was cooled to 50-60.degree., dild. with 5.0 L EtOAc, and allowed to stand

for 3 h at 20.degree. to give 920 g II contg. 0.05% III and 0.10% III.HCl.
Recrystn. of the product from 4 L EtOH gave II suitable for drug manuf. By distn. of the mother liquor after 1st crystn. 91% EtOAc and 89% DMF were regenerated.
IC ICM C07D281-02
CC 28-22 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **63**
IT **127-19-5P**, N,N-Dimethyl acetamide
RL: PREP (Preparation)
(**solvent**, diltiazem hydrochloride purifn. by crystn. from isopropanol and)

L60 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:573775 HCAPLUS
DOCUMENT NUMBER: 111:173775
TITLE: 3-Phenyl-4-hydroxybenzoic acid and its preparation
INVENTOR(S): Nakanishi, Takehisa; Miura, Toshizumi
PATENT ASSIGNEE(S): Mitsui Toatsu Chemicals, Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01113340	A2	19890502	JP 1987-268208	19871026

AB The title compd. (I), useful as material for preservatives, and arom. polyesters and intermediates for drugs and agrochems., was prepd. by treating o-PhC6H4OK (II) with CO2 in **aprotic** polar solvents. Thus, CO2 was bubbled into DMF soln. of II at 100.degree. and normal pressure for 1 h to give I with 85% selectivity and 46% conversion.
IC ICM C07C065-105
ICS C07C051-15
CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
IT Agrochemicals
Pharmaceuticals
Preservatives
(intermediate for, phenylhydroxybenzoic acid as)
IT **67-68-5**, **Dimethyl sulfoxide**, uses and miscellaneous 68-12-2, Dimethylformamide, uses and miscellaneous **127-19-5**, **Dimethylacetamide** 680-31-9, uses and miscellaneous 872-50-4, N-Methyl-2-pyrrolidone, uses and miscellaneous
RL: USES (Uses)
(**solvent**, for carboxylation of phenylphenol potassium salt)

L60 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:515057 HCAPLUS
DOCUMENT NUMBER: 111:115057
TITLE: Preparation of 2-methoxy-6-methylaminopyridine as an intermediate for drugs and agrochemicals
INVENTOR(S): Shimazu, Hidetaka
PATENT ASSIGNEE(S): Koei Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01085965	A2	19890330	JP 1987-245100	19870928

AB The title compd. (I) is prepd. by treating 6-halo-2-methylaminopyridines with MeOH in **aprotic** polar solvents in the presence of alkali hydroxides. 6-Chloro-2-methylaminopyridine was added to a mixt. of NaOH and MeOH in DMSO and the soln. was heated at 100.degree. under addn. of MeOH for 15 min and at 100-120.degree. for 16 h to give 76.3% I.
IC ICM C07D213-74
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 5
IT Agrochemicals
Pharmaceuticals
(intermediate for, methoxy(methylamino)pyridine as)
IT **67-68-5**, DMSO, uses and miscellaneous
RL: USES (Uses)
(**solvent**, for methoxylation of chloro(methylamino)pyridine)

L60 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:406916 HCAPLUS
DOCUMENT NUMBER: 111:6916
TITLE: Preparation of 1-bromo-2-fluoroethane as intermediate for drugs and agrochemicals
INVENTOR(S): Kumai, Seisaku; Yokokoji, Osamu
PATENT ASSIGNEE(S): Asahi Glass Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63284138	A2	19881121	JP 1987-117122	19870515

AB The title compd. (I) is prepd. by fluorination of BrCH2CH2Br with HF in **aprotic** polar solvent in the presence of Cu2O. A mixt. of BrCH2CH2Br and Cu2O in sulfolane was treated with HF in an autoclave at 100.degree. for 6 h to give I with 93.5% selectivity and 69.7% conversion vs. 56.5% selectivity and 42.5% conversion using THF as the solvent.
IC ICM C07C019-08
ICS B01J023-72; C07C017-20
CC 23-3 (Aliphatic Compounds)
Section cross-reference(s): 1, 5
IT Agrochemicals
Pharmaceuticals
(intermediate for, bromofluoroethane as)
IT **67-68-5**, DMSO, uses and miscellaneous
RL: USES (Uses)
(**solvent**, for fluorination of dibromoethane)

L60 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:39376 HCAPLUS
DOCUMENT NUMBER: 110:39376
TITLE: Coupling of proteins to variable groups in anhydrous media
INVENTOR(S): Levy, Julia G.; Liu, Daniel
PATENT ASSIGNEE(S): University of British Columbia, Can.
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 267038	A2	19880511	EP 1987-309809	19871105
EP 267038	A3	19890712		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 8780828	A1	19880512	AU 1987-80828	19871105
AU 598426	B2	19900621		
CA 1303292	A1	19920609	CA 1987-551178	19871105
JP 63253096	A2	19881020	JP 1987-281931	19871106
US 4843147	A	19890627	US 1988-248267	19880921
PRIORITY APPLN. INFO.:			US 1986-927847	19861106

AB Protein conjugates, useful, e.g., in prepn. of drugs, were prepd. by mixing the protein with a second component and a conjugation reagent in a polar **aprotic** solvent. Hematoporphyrin and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide were stirred 30 min in DMSO and peanut agglutinin (PNA) was added. The mixt. was stirred 2 min and dialyzed against phosphate-buffered saline to give a conjugate having 50 .mu.g hematoporphyrin/ng PNA.

IC ICM C07K003-08
ICS C07K017-00; A61K039-385

CC 34-4 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 9

IT **Pharmaceuticals**
(protein conjugates with variable groups)

IT **67-68-5, Dimethyl sulfoxide**, uses and miscellaneous
RL: USES (Uses)
(**solvent**, for anhyd. coupling of proteins to variable groups)

L60 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:630798 HCAPLUS
DOCUMENT NUMBER: 109:230798
TITLE: Preparation of N-substituted maleimides
INVENTOR(S): Inagaki, Takeshi; Takayanagi, Yasuyuki; Narita, Takeshi
PATENT ASSIGNEE(S): Nitto Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 63122666	A2	19880526	JP 1986-267777	19861112
JP 07072173	B4	19950802		

AB Title compds., useful as materials for drugs, agrochems., dyes, and polymers are prepd. in one step by treating maleic anhydride (I) with arom. or aliph. primary amines in the presence or absence of acid catalysts selected from P- or S-contg. oxo acids or org. sulfonic acids at 50-200.degree. in mixts. contg. (A) solvents (which form azeotropes with H2O) selected from benzene, toluene, xylene, PhEt, and PhCl and (B) **aprotic** polar solvent selected from HCONH2, DMF, AcNMe2, HCONHMe, DMSO, sulfolane, .gamma.-butyrolactone, and HMPA. Thus, I, xylene, DMF, and p-MeC6H4SO3H were heated at .gtoreq.100.degree., treated dropwise with PhNH2, then the mixt. was stirred for 0.5 h to give 98.5% N-phenylmaleimide without formation of polymers.

IC ICM C07D207-448

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

IT Agrochemicals
Dyes
Pharmaceuticals
Polymers, preparation
RL: PREP (Preparation)
(materials for, substituted maleimides as)

IT **67-68-5**, DMSO, uses and miscellaneous 68-12-2, Dimethylformamide, uses and miscellaneous 71-43-2, Benzene, uses and miscellaneous 75-12-7, Formamide, uses and miscellaneous 96-48-0, .gamma.-Butyrolactone 100-41-4, Ethylbenzene, uses and miscellaneous 108-88-3, Toluene, uses and miscellaneous 108-90-7, Chlorobenzene, uses and miscellaneous 123-39-7, N-Methylformamide 126-33-0, Sulfolane **127-19-5, Dimethylacetamide** 680-31-9, Hexamethylphosphoramide, uses and miscellaneous 1330-20-7, Xylene, uses and miscellaneous
RL: RCT (Reactant)
(**solvents** contg., for prepn. of substituted maleimides from maleic anhydride and amines)

L60 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:188895 HCAPLUS
DOCUMENT NUMBER: 108:188895
TITLE: Process for the manufacture of pure perfluorinated, cyano group-containing benzenes
INVENTOR(S): Nalewajek, David; Lockyer, George Donald; Eibeck, Richard Elmer; Pyszczek, Michael Francis
PATENT ASSIGNEE(S): Allied Corp., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8707267	A1	19871203	WO 1986-US2662	19861210

W: JP
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE

PRIORITY APPLN. INFO.: US 1986-864661 19860519

AB C6Fx(CN)y (x, y = integers whose sum is 6) are prepd. in high yield and purity by reacting KF and C6Clx(CN)y in a heated dipolar **aprotic** solvent. This method also provides a 1-step process for purifying the crude title compds. (esp. crude tetrafluorophthalonitrile) into a material of sufficient purity that it can be used directly in the manuf. to the pharmaceuticals. Anhyd. KF (88 g) and 50 g tetrachlorophthalonitrile were heated in 400 mL of DMF for 1.5 h at 130.degree., cooled to room temp., and poured into 1 L of H2O. The ppt. which formed was stirred for 0.5 h, filtered, and dried, producing 30.3 g of 98.5%-pure tetrafluorophthalonitrile, representing 85% yield. This crude product was dissolved in 2 L hexane and treated with 10 g activated carbon at 69.degree. for 0.5 h, hot-filtered, and cooled to ambient temp. to yield 29.9 g of 99.7%-pure tetrafluorophthalonitrile, corresponding to a product yield of 83%.

IC ICM C07C121-50
ICS C07C120-00; C07C063-68

CC 45-4 (Industrial Organic Chemicals, Leather, Fats, and Waxes)
Section cross-reference(s): 25, **63**

ST fluorophthalonitrile high purity manuf; pure tetrafluorophthalonitrile **pharmaceutical** intermediate manuf; chlorophthalonitrile potassium fluoride reaction; alkane solvent purifn tetrafluorophthalonitrile; amide solvent tetrachlorophthalonitrile conversion

IT 68-12-2, Dimethylformamide, uses and miscellaneous **127-19-5, Dimethylacetamide** 872-50-4, N-Methylpyrrolidone, uses and miscellaneous
RL: USES (Uses)
(**solvents**, for manuf. of fluoro arom. nitriles)

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=> fil wpids

FILE 'WPIDS' ENTERED AT 09:08:16 ON 26 FEB 2001
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FILE LAST UPDATED: 24 FEB 2001              <20010224/UP>
>>>UPDATE WEEKS:
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DERWENT WEEK FOR POLYMER INDEXING:  200111
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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    SEE http://www.derwent.com/covcodes.html  <<<

=> d his


     (FILE 'REGISTRY' ENTERED AT 08:32:29 ON 26 FEB 2001)
               DEL HIS Y

     FILE 'WPIDS' ENTERED AT 08:39:12 ON 26 FEB 2001
L1         31283 S GLYCEROL OR GLYCERIN# OR PROPANETRIOL OR TRIHYDROXYPROPANE
OR
L2         19385 S PEG 400 OR (POLYETHYLENE OR POLY ETHYLENE) (W) GLYCOL OR
ETHA
               E (DIMETHYLAMIDE OR DIMETHYL AMIDE OR DI METHYL AMIDE OR DI
MET
L3          3853 S (DIMETHYLAMIDE OR DIMETHYL AMIDE OR DI METHYL AMIDE OR DI
MET
               E ACETIC ACID OR VINEGAR OR ETHANOIC ACID OR ETHYLIC ACID
               E PROPYLENE GLYCOL OR PROPANE DIOL OR PROPANEDIOL OR
HYDROXYPRO
L4         16557 S PROPYLENE GLYCOL OR PROPANE DIOL OR PROPANEDIOL OR
HYDROXYPRO
               E DMSO OR DIMETHYLSULFOXIDE OR DIMETHYLSULPHOXIDE OR DI
METHYL
L5         10257 S DMSO OR DIMETHYLSULFOXIDE OR DIMETHYLSULPHOXIDE OR DI
METHYL
L6        297768 S SOLVENT#
L7          6174 S APROTIC
L8          5813 S L6 (L) L7
L9          2110 S L8 AND B/DC
L10           15 S L9 AND L1
L11           19 S L9 AND L2
L12          109 S L9 AND L3
L13           13 S L9 AND L4
L14          325 S L9 AND L5
L15        16376 S (2 OR SECOND?  OR ANOTHER OR ADDITION?) (3A) SOLVENT?
```

```
L16          393 S L10 OR L11 OR L12 OR L13 OR L14
L17           32 S L16 AND L15
L18         4919 S CASTOR OIL#
L19         2748 S (SOYBEAN OR SOY BEAN) (W) OIL#
L20            1 S L18 AND L9
L21            0 S L19 AND L9
L22          721 S PARENTAL?
L23            0 S L17 AND L22
L24         4794 S LYOPHIL?
L25            0 S L17 AND L24
L26          114 S L9 AND L15
L27            2 S L26 AND (L22 OR L24)
L28        18241 S PARENTER?
L29            0 S L28 AND L17
L30            3 S L28 AND L26
L31           36 S L17 OR L27 OR L30
L32            0 S INTERLIPID
L33           20 S INTRALIPID
L34            0 S L33 AND L6
L35           26 S L3 AND L2 AND L4 AND L6
L36           12 S L35 AND B/DC
L37            1 S L36 AND L7
L38            3 S L3 AND L2 AND L9
L39        35383 S ACETIC ACID OR VINEGAR OR ETHANOIC ACID OR ETHYLIC ACID
L40          132 S L9 AND L39
L41            7 S L40 AND L15
L42            1 S L39 AND L2 AND L9
L43           11 S L37 OR L38 OR L41 OR L42
L44           32 S L31 NOT L43

     FILE 'WPIDS' ENTERED AT 09:08:16 ON 26 FEB 2001

=> d .wp 143 1-11;d .wp 144 1-32


L43  ANSWER 1 OF 11  WPIDS COPYRIGHT 2001   DERWENT INFORMATION LTD
AN   2001-061466 [07]   WPIDS
DNC  C2001-017031
TI   Insoluble polymers to which are bonded ascorbic acid, used to remove
     oxidizing agents, e.g. iodine, from solutions, such as reaction mixtures
     as in parallel array syntheses and combinatorial chemistry.
DC   A13 A14 A89 B05 E19
IN   ZHANG, L
PA   (ELIL) LILLY & CO ELI
CYC  92
PI   WO 2000072959 A1 20001207 (200107)* EN   19p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
            EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
            LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
            SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
ADT  WO 2000072959 A1 WO 2000-US6706 20000509
PRAI US 1999-135980   19990526
AB   WO 200072959 A UPAB: 20010202
     NOVELTY - Insoluble polymers to which are bonded ascorbic acid.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
```

(1) removing an oxidizing agent from a solution comprising reacting the oxidizing agent with the polymer bonded to ascorbic acid;

(2) the preparation of the polymer.

USE - The polymers are used to remove oxidizing agents, such as iodine, chlorine, bromine, chromium oxide, chromium oxide/pyridine, selenium oxide, hydrogen peroxide and a peroxide, from solutions, such as reaction mixtures such as in parallel array syntheses and combinatorial chemistry (claimed). They are also used to prevent oxidation of compounds, including those prepared by parallel array syntheses, by storing the compounds in their presence (claimed). BisAcm-oxytocin (H-Cys(acetoamidomethyl (Acm))-Tyr-Ile-Gln-Asn-Cys(Acm)-Pro-Leu-Gly-NH2) was prepared with a Rainin Synthesizer (RTM: synthesizer) on RINK-amide resin using Fmoc-chemistry. The two cysteine thiols were protected with Acm groups. The linear peptide was removed from the resin in a solution containing trifluoroacetic acid (TFA) (94 %), anisole (2 %), triisopropylanisole (2 %) and water (2 %) (4 hours, room temperature). The linear polypeptide was precipitated with diethyl ether and purified on a preparative C18 reverse-phase high-performance liquid chromatography (HPLC) column with a linear gradient of water containing TFA (0.045 %), and acetonitrile (60 %) in water containing TFA (0.039 %) at a flow rate of 10 ml/minute followed by lyophilization of the major products. The linear polypeptide was converted to a cyclic polypeptide by Acm deprotection from the two protected cysteines of the purified linear bond and intermolecular disulfide bond formation from the resulting liberated thiols by reacting with an excess of iodine in 10 % **acetic acid** in water at room temperature for 2 hours. To remove excess iodine from the reaction mixture, L-ascorbic acid immobilized polystyrene was added directly to the reaction mixture. After 2 hours, the resin was removed by filtration. Formation of the cyclic product was confirmed by LC ESMS.

ADVANTAGE - Sensitive functional groups such as disulfides are not affected by the reaction of ascorbic acid bonded to the insoluble polymers with oxidizing agents in reaction mixtures and can thus be used to remove oxidizing agents from reaction mixtures with organic, protic or **aprotic** polar **solvents** without modifying sensitive functional groups such as disulfides. Because the polymers can be separated from reaction mixtures by simple filtration, they are suitable for use in small-scale reactions and automated procedures, particularly parallel array syntheses by which combinatorial libraries are prepared. Dwg.0/0

L43 ANSWER 2 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-184683 [17] WPIDS
CR 2000-074579 [04]
DNC C2000-058046
TI New polyamine telomers useful for gene therapy.
DC A14 A96 **B04 B05** D16
IN BOUSSIF, O; SANTAELLA, C; VIERLING, P
PA (TRGE) TRANSGENE SA
CYC 25
PI EP 965584 A2 19991222 (200017)* EN 42p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

ADT EP 965584 A2 EP 1999-111504 19990614
PRAI EP 1998-401471 19980615
AB EP 965584 A UPAB: 20000405
NOVELTY - Polyamine telomers (I) are new.
DETAILED DESCRIPTION - Polyamine telomer of formula (I) are new.
A = H, 1-4C alkyl or 5-7 aryl;
n = 1-100;
R1 = H, methyl, ethyl or -(CH2)u-B1;
x, u = 2-4;
B1 = group of formula (i) or (ii);
y = 2-4;
z = 0-6;
R3-R6 = H, 1-4C alkyl, 1-4C hydroxyalkyl.
INDEPENDENT CLAIMS are also included for:
(1) a composition comprising (I);
(2) a complex for transfering an active substance to a cell comprising at least one (I) and/or at least one of the above composition and at least one active substance (comprising at least one negative charge);
(3) tranfering in vitro at least one substance in a cell using the complex;
(4) the preparation of the complex;
(5) a pharmaceutical composition comprising the complex; and
(6) a cell transfected by the complex.
ACTIVITY - None given.
MECHANISM OF ACTION - Transfecting agent for gene therapy. A549 cells (epithelial cells derived from human pulmonary carcinoma) were cultivated in vitro and treated with DNA/telomer complex. 48 hours after transfection the culture medium was removed and washed in order to determine the luciferase activity. The results showed that the polyamines enable transfection of the plasmid into the cells.
USE - (I) are useful for transfering in vitro of at least one nucleic acid in a cell, preferably a mammalian cell. Thus (I) can be useful in composition for vaccinal treating or preventing of man and animals, and in gene therapy (claimed). The polyamine telomers can also be used for ex vivo or in vivo transfer of nucleic acid into cells.
ADVANTAGE - The polyamines enable transfection of the plasmid into the cells and that the transfection efficiency depends on the length of the polyamine chain, on the charge ratio and on the amount of DNA. The presence of an equimolar quantity of DOPE is more efficient than the use of complexes composed of strongly charged polyamines (II: L = (iv); m = 17; n = 20, 40 or 60).
Dwg.0/5

L43 ANSWER 3 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-561647 [47] WPIDS
DNC C1999-163642
TI Preparation of (R)-alpha-(2,3-dimethoxyphenyl)-1-(2-(4-fluorophenyl)ethyl)-4-piperidinemethanol - used to treat e.g. schizophrenia, cardiovascular disorders and extrapyramidal symptoms associated with neuroleptic therapy.
DC **B03**

IN BINA, A G; DAUGS, E D; EVANS, J C; FLEMMING, H; GUILLAMOT, G; HAWTHORNE, R
A; HILPERT, T H E; HITT, J E; KING, C R; KOEK, J N; LASKOVICS, F M; LEFLER, J R; MARGOLIN, A L; MINISH, S K; ORTYL, T T; RAJEWSKI, L G; SACK, M J; SKULTETY, P F; STOLZ-DUNN, S K; TIGNER, A L; TOMLINSON, I A; STOLTZ-DUNN, S K

PA (HMRI) HOECHST MARION ROUSSEL DEUT GMBH; (HMRI) HOECHST MARION ROUSSEL INC; (AVET) AVENTIS PHARM INC; (AVET) AVENTIS PHARMA DEUT GMBH

CYC 84

PI WO 9946245 A2 19990916 (199947)* EN 194p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
ZA 9901907 A 19991124 (200001) 195p
AU 9929988 A 19990927 (200006)
BR 9909260 A 20001121 (200065)
NO 2000004545 A 20001113 (200067)

ADT WO 9946245 A2 WO 1999-US5332 19990311; ZA 9901907 A ZA 1999-1907 19990309;
AU 9929988 A AU 1999-29988 19990311; BR 9909260 A BR 1999-9260 19990311, WO 1999-US5332 19990311; NO 2000004545 A WO 1999-US5332 19990311, NO 2000-4545 20000912

FDT AU 9929988 A Based on WO 9946245; BR 9909260 A Based on WO 9946245

PRAI US 1999-250718 19990216; US 1998-42251 19980313

AB WO 9946245 A UPAB: 19991116
NOVELTY - Preparation of (R)- alpha -(2,3-dimethoxyphenyl)-1-(2-(4-fluorophenyl)ethyl)-4-piperidinemethanol via new intermediates
DETAILED DESCRIPTION - The following compounds are claimed:
(a) (R)- alpha -(2,3-dimethoxyphenyl)-4-piperidinemethanol (Ia);
(b) 4-(1-oxo-1-(2,3-dimethoxyphenyl)methyl)-N-2-(4-fluorophen-1-oxoethyl)piperidine (Ib);
(c) (R)- alpha -(2,3-dimethoxyphenyl)-1-(2-(4-fluorophenyl)ethyl)-4-piperidinemethanol, (2S,3S)-(+)-di-(p-anisoyl)tartaric acid salt (Ic);
(d) 4-(1-hydroxy-1-(2,3-dimethoxyphenyl)methyl)pyridine (Id);
(e) 4-(2,3-dimethoxybenzoyl)pyridine (Ie);
(f) 4-(1-hydroxy-1-(2,3-dimethoxyphenyl)methyl)-N-2-(4-fluorophen-1-oxo-ethyl)piperidine (If);
(g) (R)- alpha -(2,3-dimethoxyphenyl)-1-(2-(4-fluorophenyl)ethyl)-4-piperidinemethanol (Ig)
having a particle size of 25-250 micro m.
INDEPENDENT CLAIMS are included for the following:
(1) the preparation of (Ig) comprising reacting (Ia) with a 4-fluorophenylethyl alkylating agent of formula (II; X = halide or methanesulfonate) or reacting (Ib) or 4-(1-oxo-1-(2,3-dimethoxyphenyl)methyl)-N-2-(4-fluorophenylethyl)piperidine (Ih) with a chiral reducing agent:
(2) the preparation of (Ig) comprising:
(a) reacting alpha -(2,3-dimethoxyphenyl)-1-(2-(4-fluorophenyl)ethyl)-4-piperidinemethanol (III) with (2S,3S)-(+)-di-(p-anisoyl)tartaric acid (IV) to give a racemic mixture of (Ic) and the corresponding (S) compound.;
(b) separating the (R)-isomer by selective crystallization;
(c) reacting (Ic) with a base;

(3) the preparation of (Ig) comprising reacting (Ic) with a base;
(4) the preparation of (Ig) comprising enzymatic hydrolysis of (III).butyrate ester to give a mixture of (Ig) and the corresponding (S) enantiomer in the form of its butyrate ester and separating (Ig).
(5) the preparation of (Ig) comprising using ethyl N-(4-fluorophenylthioacetyl)-4-carboxylpiperidine, 1-(4-carboethoxypipeidine)-2-(4-fluorophenyl)ethane or N-4-fluorophenylacetyl)-4-carboxypiperidine;
(6) preparation of 4-(1-hydroxy-1-(2,3-dimethoxyphenyl)methyl)piperidine (V) comprising catalytic hydrogenation of (Id) or reaction of 4-(2,3-dimethoxybenzoyl)pyridine with a reducing agent;
(7) preparation of (R)-4-(1-hydroxy-1-(2,3-dimethoxyphenyl)-1-piperidinecarboxylic acid, 1,1-dimethylethyl ester comprising reacting 4-(2,3-dimethoxybenzoyl)-1-piperidinecarboxylic acid, 1,1-dimethylethyl ester with a chiral reducing agent;
(8) compositions comprising (R)- alpha -(2,3-dimethoxyphenyl)-1-(2-(4-fluorophenyl)ethyl)-4-piperidinemethanol (III), lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, colloidal silicon dioxide and magnesium stearate.
ACTIVITY - Cardiovascular; Antianxiety; Antischizophrenic
MECHANISM OF ACTION - 5-Hydroxytryptamine receptor antagonist.
USE - For treatment of schizophrenia, anxiety, variant angina, anorexia nervosa, Raynaud's phenomenon, intermittent claudication, coronary or peripheral vasospasms, fibromyalgia, cardiac arrhythmia, thrombotic illness and for controlling extrapyramidal symptoms associated neuroleptic therapy.
Dwg.0/0

L43 ANSWER 4 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-095297 [08] WPIDS
DNC C1999-028043
TI Preparation of 4-alkyl-3-alkoxy-aniline derivatives - by O- or N-acylating m-aminophenol, heating in presence of Friedel-Craft's catalyst, reducing and O-alkylating, used as intermediates for quinoline and quinolone compounds.
DC **B02 B05** C02 C03
IN GALLO, R; GOZARD, J P; PORTIOLI, R; ROSSI, P P; TRIPPITELLI, S; VECCHIO, E; GOZARD, J
PA (INMR) RHONE MERIEUX SAS; (CDFA-N) CD FARMASINT SRL; (MERI-N) MERIAL
CYC 21
PI WO 9857921 A1 19981223 (199908)* FR 24p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: BR CN ES
FR 2764601 A1 19981218 (199912)
EP 994846 A1 20000426 (200025) FR
R: AT BE CH DE DK ES FR GB IE LI LU MC NL PT
BR 9810037 A 20000919 (200050)
CN 1264362 A 20000823 (200063)
ADT WO 9857921 A1 WO 1998-FR1264 19980616; FR 2764601 A1 FR 1997-7444 19970616; EP 994846 A1 EP 1998-932216 19980616, WO 1998-FR1264 19980616; BR 9810037 A BR 1998-10037 19980616, WO 1998-FR1264 19980616; CN 1264362 A
CN 1998-807249 19980616

FDT EP 994846 A1 Based on WO 9857921; BR 9810037 A Based on WO 9857921
PRAI FR 1997-7444 19970616
AB WO 9857921 A UPAB: 19990302
Preparation of 4-alkyl-3-alkoxy-aniline derivatives of formula (I) comprises: (a) O- or N-acylating m-aminophenol (II) in a single step, preferably using an acid chloride or anhydride, to form a compound of formula (III);
(b) heating (III) in the presence of a Friedel-Crafts catalyst, preferably aluminium chloride to form (IV) by a Fries rearrangement; (c) selectively reducing (IV), preferably by hydrogenation in the presence of palladium on charcoal catalyst to form (V); (d) O-alkylating (V), preferably using an acid chloride and removing the protecting group on the amine function by base hydrolysis to give (I). R1 = 1-10C alkyl or aralkyl in which the alkyl group has 1-3C atoms and the aryl group is phenyl optionally substituted by 1 or 2 1-3C alkyl, at least 1 halo or by at least 1 NO2 and R2 = 1 - 16C alkyl.
A stoichiometric amount of acylating agent is used, preferably at least 2 (especially 2.2) equivalents. Reaction is effected at 100-200 deg. C for 1-2 hours. The **solvent** used is the carboxylic acid from which the acylating agent is derived. 2 equivalents of the catalyst are used per equivalent of the m-amino phenol. The reaction is effected in a **solvent** such as nitrobenzene, dichloromethane, 1,2-dichloroethane, chlorobenzene or preferably dichlorobenzene. Hydrogenation is effected at a pressure of 4-20 (especially 12) bars using 1-2 wt.% palladium per part product to be hydrogenated. Hydrogenation is effected in a lower alcohol, preferably methanol or ethanol at 50-100 (preferably 85) deg. C in the presence of an acid, especially 0.5-2.5% phosphoric, sulphuric or **acetic acid**. Alkylation is effected using a chloride of formula R1-Cl in the presence of a base in an **aprotic solvent** such as acetone, acetonitrile or dimethyl formamide (DMF) at 60 deg. C.
USE - (I) are used in the preparation of quinoline and quinolone derivatives useful in human and animal medicine, particularly methyl 7-benzyloxy-6-butyl-1,4-dihydro-4-oxo-3-quinoline carboxylate (Methylbenzoquate) used as a commercial anticoccidial agent.
ADVANTAGE - The process is cheaper and simpler to carry out commercially than known methods of preparing (I).
Dwg.0/0

L43 ANSWER 5 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1993-019706 [03] WPIDS
DNC C1993-008909
TI Chloro-fluoro-nitro-benzene prodn. from di chloro cpd. - by reaction with alkali metal fluoride in presence of volatile **aprotic solvent** and phase-transfer catalyst.
DC **B05** C03
IN KANSCHIK-CONRADSEN, A; PAPENFUHS, T; PRESSLER, W
PA (FARH) HOECHST AG
CYC 11
PI EP 523671 A2 19930120 (199303)* DE 4p
R: BE CH DE ES FR GB IT LI NL

EP 523671 A3 19930303 (199349)
JP 06157426 A 19940603 (199427) 5p
US 5463148 A 19951031 (199549) 3p
EP 523671 B1 19960117 (199608) DE 5p
R: BE CH DE ES FR GB IT LI NL
DE 59205077 G 19960229 (199614)
ES 2083631 T3 19960416 (199623)
JP 2501723 B2 19960529 (199626) 4p

ADT EP 523671 A2 EP 1992-112099 19920715; EP 523671 A3 EP 1992-112099 19920715; JP 06157426 A JP 1992-188070 19920715; US 5463148 A Cont of US 1992-914296 19920715, US 1994-238582 19940505; EP 523671 B1 EP 1992-112099 19920715; DE 59205077 G DE 1992-505077 19920715, EP 1992-112099 19920715; ES 2083631 T3 EP 1992-112099 19920715; JP 2501723 B2 JP 1992-188070 19920715

FDT DE 59205077 G Based on EP 523671; ES 2083631 T3 Based on EP 523671; JP 2501723 B2 Previous Publ. JP 06157426

PRAI DE 1991-4123600 19910717

AB EP 523671 A UPAB: 19970502
Prodn. of chlorofluoronitrobenzenes (I) is effected by reacting dichloronitrobenzenes (II) with an alkali metal fluoride (III) at 125-200 deg.C in the presence of an **aprotic solvent** and a catalyst. (III) has a water content of up to 2.5 wt.%. The catalyst is a quat. ammonium or phosphonium salt, a crown ether or a **polyethylene glycol** dimethyl ether. The **solvent** has a b.pt. below the reaction temp. at the pressure employed.
The reaction is effected with KF, RbF or CsF at 140-190 deg.C. The **solvent** is xylene, o-dichlorobenzene, 2-chlorotoluene, DMSO, **dimethylacetamide** or DMF. The (II):(III) molar ratio is 1.05-1.7:1. The catalyst is a quat. ammonium or phosphonium chloride or bromide and is used in an amt. of 2-5 wt.% based on (II).
USE/ADVANTAGE - (I) are intermediates for pharmaceuticals and plant protection agents. The process gives high yields (e.g. 57-81%) in shorter reaction times than prior art processes (cf. DE 2938939) without the need to use anhydrous (II
Dwg.0/0

L43 ANSWER 6 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1993-019703 [03] WPIDS
DNC C1993-008907
TI Di fluoro-benzaldehyde prodn. from di chloro-benzaldehyde - by reaction with alkali metal fluoride in presence of glycol ether catalyst, used as intermediates for pharmaceuticals and plant protection agents.
DC **B05** C03
IN KANSCHIK-CONRADSEN, A; PAPENFUHS, T
PA (FARH) HOECHST AG; (CLRN) CLARIANT GMBH
CYC 12
PI EP 523668 A2 19930120 (199303)* DE 4p
R: BE CH DE ES FR GB IT LI NL
US 5191126 A 19930302 (199311) 3p
JP 05213810 A 19930824 (199338) 4p
EP 523668 A3 19930428 (199401)
EP 523668 B1 19951025 (199547) DE 6p
R: BE CH DE ES FR GB IT LI NL
DE 59204105 G 19951130 (199602)
ES 2080996 T3 19960216 (199614)
EP 523668 B2 19990825 (199939) DE

R: BE CH DE ES FR GB IT LI NL
KR 214900 B1 19990802 (200104)
ADT EP 523668 A2 EP 1992-112096 19920715; US 5191126 A US 1992-913150 19920714; JP 05213810 A JP 1992-188071 19920715; EP 523668 A3 EP 1992-112096 19920715; EP 523668 B1 EP 1992-112096 19920715; DE 59204105 G DE 1992-504105 19920715, EP 1992-112096 19920715; ES 2080996 T3 EP 1992-112096 19920715; EP 523668 B2 EP 1992-112096 19920715; KR 214900 B1 KR 1992-12592 19920715
FDT DE 59204105 G Based on EP 523668; ES 2080996 T3 Based on EP 523668
PRAI DE 1991-4123461 19910716
AB EP 523668 A UPAB: 19940217
Prodn. of 2,4-difluorobenzaldehyde (Ia) or 2,6-difluorobenzaldehyde (Ib) is effected by reacting 2,4- dichlorobenzaldehyde (IIa) or 2,6-dichlorobenzaldehyde (IIb) with an alkali metal fluoride at 160-250 deg.C in a polar **aprotic solvent** in the presence of a **(poly)ethylene glycol** dialkyl ether of formula RO(CH2CH2O)nR (III) as catalyst. In (III), R = 1-3C alkyl and n = 1-50.

The reaction is pref. effected with KF, RbF or CsF at 200-230 deg.C. The **solvent** is sulpholane, DMSO, tetramethylene sulphoxide, diphenyl sulphone, **dimethylacetamide**, DMF or NMP. (III) is tetramethylene glycol dimethyl ether (IIIa) or a **polyethylene glycol** dimethyl ether with an average mol.wt. of 250, 500, 1000 or 2000.

USE/ADVANTAGE - Used are intermediates for pharmaceuticals and plant protection agents. The process gives high yields (e.g. 70-74%) without using expensive tetraphenylphosphonium bromide (cf. EP 289942 Dwg.0/6

L43 ANSWER 7 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-270791 [33] WPIDS
DNC C1992-120712
TI New mono ester(s) of saccharose - are produced with good yield and purity by acylation of saccharose and isomerisation.
DC **B03** C02 D21 E13
IN BACZKO, K; CHAUVIN, C; DURAND, P; PLUSQUELLEC, D
PA (ISOC-N) ISOCHEM SA
CYC 1
PI FR 2670493 A1 19920619 (199233)* 21p
ADT FR 2670493 A1 FR 1990-15625 19901213
PRAI FR 1990-15625 19901213
AB FR 2670493 A UPAB: 19931025
A.i) New monoesters of 2-O-acylsaccharoses (I) are claimed. R = 1-17C straight or branched, satd., aliphatic chain, or an unsatd. chain, or an aromatic gp., or a more complex gp.: (i), (ii), Ph2CH-, Ph-(CH2)2-, Ph-(CH2)3-, or Ph-CO-(CH2)2-. ii) New monoesters 6-O-acylsaccharoses (II) obtd. from the cpd. (I) above or directly from saccharose are claimed.

B.i) Prepn. of cpds. (I) by direct acylation of the free saccharose, in the presence of a base as initiator, in a polar **aprotic solvent**, followed by neutralisation of the base with **acetic acid** and isolation of the cpd. (I) by evapn. of the **solvent** under reduced pressure and recrystallisation from acetone or ethyl acetate, is claimed.

Pref. acylating agents = N-acylthiazolidine-2-thiones, imidazolides, 8-hydroxyquinoline esters, N-hydroxysuccinamide and 3-acyl-5-methyl-(3H)-1,3,4-thiadiazole-2-thiones, pref. N-acylthiazolidine-2-thiones. **Solvent** = pyridine, DMF, NMP, DMA or DMSO, pref. anhydrous DMF.

Base = sodium hydroxide, sodium methoxide, sodium or potassium t-butoxide or thiazolidine-2-thione anion, pref. sodium hydride at 0.0125-0.025 equiv., or the base can be replaced by triethylamine in excess of by 1,8-bis(dimethylamino)naphthalene. Temp. = room temp.. Time = 1-4 hrs.. ii) Cpds. (II) are prepd. from cpds. (I) by successive isomerisations, passing via the 3-O-acylsaccharoses: 2-O-acylsaccharoses, 3-O-acylsaccharoses, 6-O-acylsaccharoses.

a) Isomerisation is effected by the addn. of water and excess of a strong organic base, pref. DBU or DBN and takes 10-20 hrs. at room temp.. The base is neutralised with **acetic acid**, the **solvent** evapd. under reduced pressure and the residue recrystallised form methanol or isopropylacetate. b) Saccharose is acylated by N-acylthiazoline-2-thiones in the presence of triethylamine followed by isomerisation by DBU, taking several hrs. at room temp.. c) Saccharose is acylated in position 6 by N-acylthiazoline-2-thiones in the presence of DBU or DBN, taking 15-24 hrs. at room temp..

USE/ADVANTAGE - Saccharose monoesters have varied use in the farming industry, pharmaceuticals, cosmetics and the textile industry. Some applications require well-defined cpds., not the mixts. obtd. by transesterification of saccharose by fatty acid methyl esters or the cpds.
mixed with bi-prods. obtd. from saccharose by other chemical methods of prior arts. The claimed methods give good yields (40-60% for cpds. (II)) and excellent selectivity.
0/0
Dwg.0/0

L43 ANSWER 8 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1984-128003 [21] WPIDS
DNC C1984-053950
TI 14-Hydroxy-steroid 17-E-acrylic acid ester(s) - with positive inotropic activity prepd. by Horner reaction of 17-carbox aldehyde(s) with di ethyl phosphono-**acetic acid** ester(s).
DC **B01**
IN CHEMNITIUS, K H; HEINZE, A; HUEBLER, D; LEMKE, I; PONSOLD, K; SCHOENECKE, B; SCHUBERT, G; WUNDERWALD, M
PA (DEAK) AKAD WISSENSCHAFTEN DDR
CYC 1
PI DD 206381 A 19840125 (198421)* 9p
ADT DD 206381 A DD 1982-242699 19820823
PRAI DD 1982-242699 19820823
AB DD 206381 A UPAB: 19930925
Cpds. (I) are prepd. from cpds. (II) by Horner reaction with esters (III) in a dipolar **aprotic solvent** or **solvent** mixture with the **addition** of a strong base. The product opt. is converted by trans-esterification into a 3 beta, 14 beta-dihydroxy-steroid
17 beta-E-acrylic acid alkyl ester, which in turn may be 3-acylated with an acid deriv. or with an organic isocyanate: In formulae Z is a residue (Ia), (Ib), (Ic)a (Id); in which X is O or NH and R is H, alkyl, acyl, alkylsulphonyl, arylsulphonyl, or alkyl- or arylcarbamoyl).

The cpds. inhibit guinea-pig heart ATP-ase in vitro and exert a positive inotropic effect in vivo. The arrhythmogenic dosage is higher than that of digitoxigenin.
0/0

L43 ANSWER 9 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1978-84128A [47] WPIDS
TI Para-hydroxybenzyl cyanide prepn. - by treatment of para-hydroxy-mandelic acid with cyanide ions.
DC **B05**
PA (ICIL) IMPERIAL CHEM IND LTD
CYC 12
PI BE 867288 A 19781120 (197847)*
US 4154757 A 19790515 (197922)
ZA 7802656 A 19790810 (197942)
DE 2820853 A 19791122 (197948)
NL 7805437 A 19791121 (197949)
DK 7802122 A 19791203 (198001)
JP 54148747 A 19791121 (198001)
SE 7805274 A 19791210 (198001)
FI 7801546 A 19800131 (198009)
FR 2426676 A 19800125 (198010)
CH 633526 A 19821215 (198303)
CH 633529 A 19821215 (198303)
IT 1174364 B 19870701 (199025)#
PRAI BE 1978-867288 19780519
AB BE 867288 A UPAB: 19930901
p-Hydroxy benzyl cyanide (I) is prepd. by reaction of p-hydroxy mandelic acid (i.e. alpha-hydroxy-alpha-(p-hydroxyphenyl)**acetic acid**) (II) with a cyanide ion. The cyanide ion is usually derived fro an alkali metal cyanide, esp. NaCN. The reaction is effected either in a high boiling dipolar **aprotic solvent**, such as DFM, **2**-pyrrolidone, N-methyl-2-pyrrolidone, or DMSO, at 120-190 (pref. 135) degrees C of in a lower boiling **solvent**, such as methanol or methanol/dimethoxyethane, in the presence of a formic ester.
(I) is an intermediate used in the prepn. of the known beta-adrenergic blocking agent, atenolol p-(2-hydroxy-3-isopropylamino propoxy) phenylacetamide (III).

L43 ANSWER 10 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1978-84126A [47] WPIDS
TI Para-hydroxybenzyl cyanide prepn. - by treatment of alpha-para-hydroxyphenyl glycine with cyanide ions.
DC **B05**
PA (ICIL) IMPERIAL CHEM IND LTD
CYC 11
PI BE 867286 A 19781120 (197847)*
US 4154758 A 19790515 (197922)
ZA 7802654 A 19790809 (197942)
DE 2820852 A 19791122 (197948)
NL 7805435 A 19791121 (197949)
DK 7802120 A 19791203 (198001)
JP 54148744 A 19791121 (198001)
SE 7805272 A 19791210 (198001)
FI 7801544 A 19800131 (198009)
FR 2426675 A 19800125 (198010)
IT 1158713 B 19870225 (198912)
PRAI BE 1978-867286 19780519
AB BE 867286 A UPAB: 19930901
p-Hydroxybenzyl cyanide (I) is prepd. by reaction of alpha-(p-hydroxyphenyl)glycine (II) (i.e. alpha-amino-alpha-(p-hydroxyphenyl) **acetic acid**), with a cyanide ion. The cyanide ion is pref. derived from an alkali metal cyanide, such as NaCN or KCN, and the

reaction is effected in a high boiling dipolar **aprotic solvent** such as DMF, **2**-pyrrolidone, N-methyl-2-pyrrolidone, DMSO, n-butanol, 3-methyl butanol, acetamide, 2-ethoxyethanol, water, ethylene glycol formamide or urea.

(I) is an intermediate for p-2-hydroxy-3-isopropylaminopropoxy)phenylacetamide (III) a known beta-adrenergic blocking agent.

L43 ANSWER 11 OF 11 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1970-77654R [42] WPIDS
TI Isomerisation of 17-beta hydroxysteriod - via the sulphonates.
DC **B01**
PA (ORGA) ORGANON NV
CYC 8
PI NL 6905418 A (197042)*
DE 2016783 A (197044)
FR 2042311 A (197116)
CA 891489 A (197206)
US 3652605 A (197217)
GB 1304415 A (197304)
JP 48011092 B (197315)
CH 534141 A (197322)
DE 2016783 B 19771020 (197743)
NL 162658 B 19800115 (198006)
PRAI NL 1969-5418 19690408
AB NL 6905418 A UPAB: 19930831
17 beta-Hydroxysteroids are converted to their 17 alpha-analogues by (a) formation of a 17 beta-sulphonate, (b) reacting the sulphonate with an alkali metal 1. alkanoate (pref. acetate) and lower alkanoic acid (pref. **acetic acid**) in the ratio 1:0.5-**2**, in an **aprotic solvent** (pref. D.M.F.), and (c) hydrolysing the resultant 17 alpha-acyloxy deriv.

Thus testosterone-17 beta-tosylate (1 g), heated 4 hr. at 160 degrees with EtCO2K (5g) and EtCO2H (3.3 ml) in N-methyl-pyrrolidone (20 ml), followed by saponification with 20% NaOH (6 ml) in EtOH (20 ml), gave 17-epitestosterone.

L44 ANSWER 1 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-093809 [11] WPIDS
DNC C2001-027838
TI Production of 3-amino-2-hydroxy-butyric acid derivative used as intermediates for pharmaceuticals by reacting 2-amino-propionaldehyde derivative with metal cyanide and treating with acid.
DC **B02 B05** C02 C03
IN FURUKAWA, Y; HINOUE, K; YAEGASHI, K
PA (OSAS) DAISO CO LTD
CYC 26
PI EP 1063232 A2 20001227 (200111)* EN 14p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2312385 A1 20001222 (200111) EN
ADT EP 1063232 A2 EP 2000-401792 20000622; CA 2312385 A1 CA 2000-2312385 20000621

PRAI JP 1999-174967 19990622
AB EP 1063232 A UPAB: 20010224
NOVELTY - Production of an erythro-3-amino-2-hydroxybutyronitrile derivative (III) comprises reacting a 2-aminoaldehyde derivative (I) with a metal cyanide in the presence of an acid chloride and/or an acid anhydride or reacting with an organic cyanide in the presence of a Lewis acid to give stereoselectively a erythro-3-amino-2-hydroxybutyronitrile derivative (II) and treating (II) with an acid.
DETAILED DESCRIPTION - Production of an erythro-3-amino-2-hydroxybutyronitrile derivative of formula (III) comprises:
(1) reacting a 2-aminoaldehyde derivative of formula (I) with a metal cyanide in the presence of an acid chloride and/or an acid anhydride or reacting with an organic cyanide in the presence of a Lewis acid to give stereoselectively a erythro-3-amino-2-hydroxybutyronitrile derivative of formula (II) and
(2) treating (II) with an acid in water or water containing solvent to give (III) or treating (II) with an acid in alcoholic solvent of formula R3'OH to form an ester of (III).
R1 = 1-6C straight-chain, branched or cyclic alkyl, 1-8C alkylthio, 1-8C arylthio or optionally substituted aryl;
P1, P2 = aralkyl, aralkyloxycarbonyl, arylcarbonyl, or arylsulfonyl (all optionally substituted), or
P1 + P2 = optionally substituted phthaloyl or naphthaloyl ring and
R2 = alkylcarbonyl or optionally substituted arylcarbonyl;
R3 = H;
R3' = straight chain, branched or cyclic 1-6C alkyl or optionally substituted aralkyl;
Q1, Q2 = H, or optionally substituted aralkyl or arylsulfonyl, or
Q1 + Q2 = optionally substituted phthaloyl or naphthaloyl.
INDEPENDENT CLAIMS are included for the following:
(1) production of (II) by step (1) as above and
(2) production of (III) by step (2) as above.
USE - (III) Are Used as synthetic intermediates of medicines and agrochemicals.
ADVANTAGE - The process produces (I) having the desired configuration in high yields and high selectivity.
Dwg.0/0

L44 ANSWER 2 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-091197 [10] WPIDS
DNC C2001-026812
TI Preparation of pure 5'-protected deoxyribonucleosides in polar solvents, is suitable for scaling up and avoids large scale use of pyridine, DMAP, and chromatography.
DC **B02 B03**
IN KOCUR, M A; LI, X C; MA, J; MASILAMANI, D; TRUE, W R; WU, C C
PA (ALLC) ALLIED-SIGNAL INC
CYC 83
PI WO 2000075154 A2 20001214 (200110)* EN 45p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW

ADT WO 2000075154 A2 WO 2000-US15287 20000602
PRAI US 1999-444184 19991119; US 1999-137639 19990604
AB WO 200075154 A UPAB: 20010220
NOVELTY - Preparation of pure 5'-protected deoxyribonucleosides (DN), by first N-acylating in a polar **solvent** free from pyridine, dissolving the N-protected DN in a polar **aprotic solvent** and reacting with protecting reagent; then removing polar impurities by liquid-liquid extraction and non-polar impurities by solidification.

DETAILED DESCRIPTION - Preparation of a pure 5'-protected deoxyribonucleoside (DN), comprising: (a) dissolving the input DN, having any exocyclic amino groups protected, in an inert polar **aprotic solvent**; (b) reacting with the protecting reagent to form the 5'-protected DN of formula (I); (c) removing polar impurities by one or more liquid-liquid extractions using polar and non-polar **solvents** so that the (I) partitions preferentially into the non-polar phase and impurities into the polar phase; (d) separating the non-polar phase; (e) removing non-polar impurities by solidifying (I) out of solution to leave dissolved non-polar impurities; and optionally (f) recovering (I); is new.

An INDEPENDENT CLAIM is also included for selective protection of exocyclic amino groups in a DN without protection of the DN hydroxy groups, comprising: (a) dispersing the input DN requiring exocyclic amino group protection in a polar **solvent** free from pyridine, and which dissolves the N-protected DN; and (b) acylating selectively.

USE - The processes provide an economic synthesis of N-protected DN and their 5'-protected derivatives (I) suitable for scale up to industrial quantities; the examples are on hundreds of gram scale. The use of (I) as intermediates in oligo- and polynucleotide syntheses, and the uses of these products, are well known to workers in this area, and demand for them is growing.

ADVANTAGE - The processes are unhampered by scale limiting reagents and techniques of prior art. Particularly, noxious and toxic pyridine, which had to be used in relatively large amounts and is difficult to rid the product of and dispose of, is not required; neither is toxic DMAP as catalyst. Chromatography, which requires enormous investment for start up on a large scale and results in a need to dispose of or recycle large amounts of **solvents**, is likewise dispensed with.

Dwg.0/4

L44 ANSWER 3 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-679546 [66] WPIDS
DNC C2000-206690
TI New method of preparation of mirtazapine, recrystallization from a crude product and preparation of an intermediate..
DC **B02**
IN FINKELSTEIN, N; LIBERMAN, A; SINGER, C
PA (FINK-I) FINKELSTEIN N; (LIBE-I) LIBERMAN A; (SING-I) SINGER C; (TEVA-N) TEVA PHARM IND LTD; (TEVA-N) TEVA PHARM USA INC
CYC 91
PI WO 2000062782 A1 20001026 (200066)* EN 22p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000043577 A 20001102 (200107)
ADT WO 2000062782 A1 WO 2000-US10357 20000418; AU 2000043577 A AU 2000-43577 20000418
FDT AU 2000043577 A Based on WO 200062782
PRAI US 1999-130047 19990419
AB WO 200062782 A UPAB: 20001219
NOVELTY - Preparation of mirtazapine (I) comprises reacting a 2-amino-3-substituted pyridine with an N-methyl-1-phenyl-2,2'-iminodiethyl halide to give a 1-(3-substituted pyridyl)-4-methyl-2-phenyl-piperazine to which a ring closing reagent is added to give mirtazapine.
DETAILED DESCRIPTION - Preparation of mirtazapine comprises reacting a 2-amino-3-substituted pyridine of formula (II) with an N-methyl-1-phenyl-2,2'-iminodiethyl halide of formula (III) to give a compound of formula (IV). Compound (IV) is then reacted with a ring closing reagent to give mirtazapine of formula (I).
R1 = hydroxymethyl, chloromethyl, bromomethyl or iodomethyl;
R2 = amine; and
R3 = halo.
INDEPENDENT CLAIMS are also included for:
(a) preparation of 1-(3-carboxypyridyl-2)-4-methyl-2-phenyl-piperazine by hydrolyzing 1-(3-cyanopyridyl-2)-4-methyl-2-phenyl piperazine in the presence of up to 12 equivalents of base; and
(b) recrystallization of mirtazapine by: (1) heating a mixture of crude mirtazapine and a **solvent**; (2) cooling the mixture to precipitate purified mirtazapine; and (3) isolating recrystallized mirtazapine.
ACTIVITY - Antidepressant.
MECHANISM OF ACTION - None given.
USE - For treating depression (claimed). 1-(3-carboxypyridyl-2)-4-methyl-2-phenyl-piperazine is an intermediate in the preparation of mirtazapine.
ADVANTAGE - The present process is advantageous over previous processes in that there is a higher yield and a smaller number of steps in the process and the raw material costs are minimized.
Dwg.0/0

L44 ANSWER 4 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-636439 [61] WPIDS
DNC C2000-192160
TI Preparation of 4-((3-ethynyl)phenylamino) quinazoline derivatives, used to treat cancers, comprises reacting protected derivative with metal hydroxide in alkanol or with tetraalkylammonium salt in **aprotic solvent**.
DC **B02**
IN LEHNER, R S; NORRIS, T; SANTAFIANOS, D P; DINOS, P S
PA (PFIZ) PFIZER PROD INC
CYC 30
PI NO 2000001648 A 20001002 (200061)*
AU 2000022620 A 20001005 (200061)
SK 2000000444 A3 20001009 (200061)
EP 1044969 A2 20001018 (200062)B EN 21p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

CA 2302965 A1 20000930 (200063) EN
JP 2000290262 A 20001017 (200102) 15p
ADT NO 2000001648 A NO 2000-1648 20000330; AU 2000022620 A AU 2000-22620 20000328; SK 2000000444 A3 SK 2000-444 20000327; EP 1044969 A2 EP 2000-302256 20000320; CA 2302965 A1 CA 2000-2302965 20000329; JP 2000290262 A JP 2000-91300 20000329
PRAI US 1999-127072 19990331
AB EP 1044969 A UPAB: 20001130 ABEQ treated as Basic
NOVELTY - Preparation of 4-((3-ethynyl)phenylamino)quinazoline derivatives
(I) comprises reacting an alkynyl protected 4-((3-ethynyl)phenylamino)quinazoline derivative (II) with an alkali(ne earth) metal hydroxide in a hydroxy-substituted 1-10C alkane or with a tetra-(1-6C alkyl)-ammonium fluoride in an **aprotic solvent**.
DETAILED DESCRIPTION - Preparation of 4-((3-ethynyl)phenylamino)quinazoline derivatives of formula (I) comprises reacting an alkynyl protected 4-((3-ethynyl)phenylamino)quinazoline derivative of formula (II) with either:
(a) an alkali(ne earth) metal hydroxide in a hydroxy-substituted 1-10C alkane as **solvent** when G is C(OH)R3R4; or
(b) a tetra-(1-6C alkyl)-ammonium fluoride in an **aprotic solvent** when G is SiR3R4R5.
R1, R2 = 1-10C alkyl or 1-10C alkoxy (both optionally substituted by up to 2 of OH and 1-6C alkoxy);
R15 = H, 1-10C alkyl, or -(CH2)q(6-10C aryl);
q = 0-4;
G = -C(OH)R3R4 or SiR3R4R5; and
R3-R5 = 1-6C alkyl.
INDEPENDENT CLAIMS are also included for:
(1) preparation of (II) comprising reacting a 4-chloroquinazoline derivative of formula (III) with a protected 3-ethynylaniline derivative of formula (IV);
(2) preparation of (III) comprising reacting a 4-hydroxyquinazoline derivative of formula (V) with thionyl chloride in anhydrous dichloromethane;
(3) preparation of 4-((3-ethynyl)phenylamino)quinazoline derivatives of formulae (VI) and (VII) comprising reacting a protected 4-((3-ethynyl)phenylamino)quinazoline derivative of formula (VIII) with a primary or secondary alcohol R7-OH in the presence of an alkali metal hydroxide or alkaline earth hydroxide;
(4) preparation of 4-phenylaminoquinoxaline derivatives of formula (IX) or a salt or solvate comprising reacting another 4-phenylaminoquinoxaline derivative of formula (X) with R7-OH in the presence of an alkali metal hydroxide or alkaline earth hydroxide; and
(5) compounds (II).
R6 = 1-10C alkyl or -(CH2)mO(CH2)nCH3;
R7 = 1-10C alkyl or -(1-6C alkyl)(6-10C aryl) (both optionally substituted by 1-3 of halo, nitro, trifluoromethyl, trifluoromethoxy, (1-6C alkyl)sulfonyl, 1-6C alkyl, 1-6C alkoxy, 1-10C aryloxy or 6-10C arylsulfonyl);
m = 1-6;
n = 0-3;
G1 = -C(OH)R3R4;
R8-R10 = H, 1-10C alkyl, halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -OR11, -C(O)R11, -C(O)OR11, -NR12C(O)OR14, -C(O)R11, -NR12SO2R14, -SO2NR11R12, -NR12C(O)R11,

-C(O)NR11R12, -NR11R12, -S(O)j(CH2)q(6-10C aryl), -S(O)j(1-6C alkyl), -(CH2)q(6-10C aryl), -O(CH2)q(6-10C aryl), -NR12(CH2)q(6-10C aryl) or -(CH2)q(4-10 membered heterocycle) (the alkyl group optionally contains 1 or 2 hetero moieties selected from O, -S(O)j-, and -N(R12)-, with the proviso that 2 O atoms, or an O and S atom are not attached directly to each other, the aryl and heterocyclic are optionally fused to a 6-10C aryl group, a 5-8C saturated cyclic group, or a 4-10 membered heterocyclic group, and the alkyl, aryl and heterocyclic groups are optionally substituted by 1-5 substituents selected from halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -NR12SO2R14, -SO2NR11R12, -C(O)R11, -C(O)OR11, -OC(O)R11, NR12C(O)OR14, -NR12C(O)R11, -C(O)NR11R12, -NR11R12, -OR11, 1-10C alkyl, -(CH2)q(6-10C aryl), and -(CH2)q(4-10 membered heterocyclic);

R11 = H, 1-10C alkyl, -(CH2)q(6-10C aryl), or -(CH2)q(4-10 membered heterocyclic) (the alkyl group optionally includes 1 or 2 hetero moieties selected from O, -S(O)j-, and -N(R12)-, with the proviso that 2 O atoms, 2 S atoms, or an O and S atom are not attached directly to each other; the aryl and heterocyclic R11 groups are optionally fused to a 6-10C aryl group, a 5-8C saturated cyclic group, or a 4-10 membered heterocyclic group; the foregoing R11 substituents, except H, are optionally substituted by 1-5 substituents selected from halo, cyano, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -C(O)R12, -C(O)OR12, --OC(O)R12, -NR12C(O)R13, -C(O)NR12R13, -NR12R13, hydroxy, 1-6C alkyl, and 1-6C alkoxy);

j = 0-2;

R12, R13 = H or 1-6C alkyl; and

R14 = R11, but not H;

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Inhibitors of the erbB family of oncogenic and protooncogenic protein tyrosine kinases.

USE - (I) are useful in the treatment of hyperproliferative disorders such as cancers.

Dwg.0/0

AB NO 200001648 A UPAB: 20001205

NOVELTY - Preparation of 4-((3-ethynyl)phenylamino)quinazoline derivatives (I) comprises reacting an alkynyl protected 4-((3-ethynyl)phenylamino)quinazoline derivative (II) with an alkali(ne earth) metal hydroxide in a hydroxy-substituted 1-10C alkane or with a tetra-(1-6C alkyl)-ammonium fluoride in an **aprotic solvent**.

DETAILED DESCRIPTION - Preparation of 4-((3-ethynyl)phenylamino)quinazoline derivatives of formula (I) comprises reacting an alkynyl protected 4-((3-ethynyl)phenylamino)quinazoline derivative of formula (II) with either:

(a) an alkali(ne earth) metal hydroxide in a hydroxy-substituted 1-10C alkane as **solvent** when G is C(OH)R3R4; or

(b) a tetra-(1-6C alkyl)-ammonium fluoride in an **aprotic solvent** when G is SiR3R4R5.

R1, R2 = 1-10C alkyl or 1-10C alkoxy (both optionally substituted by up to 2 of OH and 1-6C alkoxy);

R15 = H, 1-10C alkyl, or -(CH2)q(6-10C aryl);

q = 0-4;

G = -C(OH)R3R4 or SiR3R4R5; and
R3-R5 = 1-6C alkyl.
INDEPENDENT CLAIMS are also included for:
(1) preparation of (II) comprising reacting a 4-chloroquinazoline derivative of formula (III) with a protected 3-ethynylaniline derivative of formula (IV);
(2) preparation of (III) comprising reacting a 4-hydroxyquinazoline derivative of formula (V) with thionyl chloride in anhydrous dichloromethane;
(3) preparation of 4-((3-ethynyl)phenylamino)quinazoline derivatives of formulae (VI) and (VII) comprising reacting a protected 4-((3-ethynyl)phenylamino)quinazoline derivative of formula (VIII) with a primary or secondary alcohol R7-OH in the presence of an alkali metal hydroxide or alkaline earth hydroxide;
(4) preparation of 4-phenylaminoquinoxaline derivatives of formula (IX) or a salt or solvate comprising reacting another 4-phenylaminoquinoxaline derivative of formula (X) with R7-OH in the presence of an alkali metal hydroxide or alkaline earth hydroxide; and
(5) compounds (II).
R6 = 1-10C alkyl or -(CH2)mO(CH2)nCH3;
R7 = 1-10C alkyl or -(1-6C alkyl)(6-10C aryl) (both optionally substituted by 1-3 of halo, nitro, trifluoromethyl, trifluoromethoxy, (1-6C alkyl)sulfonyl, 1-6C alkyl, 1-6C alkoxy, 1-10C aryloxy or 6-10C arylsulfonyl);
m = 1-6;
n = 0-3;
G1 = -C(OH)R3R4;
R8-R10 = H, 1-10C alkyl, halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -OR11, -C(O)R11, -C(O)OR11, -NR12C(O)OR14, -C(O)R11, -NR12SO2R14, -SO2NR11R12, -NR12C(O)R11, -C(O)NR11R12, -NR11R12, -S(O)j(CH2)q(6-10C aryl), -S(O)j(1-6C alkyl), -(CH2)q(6-10C aryl), -O(CH2)q(6-10C aryl), -NR12(CH2)q(6-10C aryl) or -(CH2)q(4-10 membered heterocycle) (the alkyl group optionally contains 1 or 2 hetero moieties selected from O, -S(O)j-, and -N(R12)-, with the proviso that 2 O atoms, or an O and S atom are not attached directly to each other, the aryl and heterocyclic are optionally fused to a 6-10C aryl group, a 5-8C saturated cyclic group, or a 4-10 membered heterocyclic group, and the alkyl, aryl and heterocyclic groups are optionally substituted by 1-5 substituents selected from halo, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -NR12SO2R14, -SO2NR11R12, -C(O)R11, -C(O)OR11, -OC(O)R11, NR12C(O)OR14, -NR12C(O)R11, -C(O)NR11R12, -NR11R12, -OR11, 1-10C alkyl, -(CH2)q(6-10C aryl), and -(CH2)q(4-10 membered heterocyclic);
R11 = H, 1-10C alkyl, -(CH2)q(6-10C aryl), or -(CH2)q(4-10 membered heterocyclic) (the alkyl group optionally includes 1 or 2 hetero moieties selected from O, -S(O)j-, and -N(R12)-, with the proviso that 2 O atoms, 2 S atoms, or an O and S atom are not attached directly to each other; the aryl and heterocyclic R11 groups are optionally fused to a 6-10C aryl group, a 5-8C saturated cyclic group, or a 4-10 membered heterocyclic group; the foregoing R11 substituents, except H, are optionally substituted by 1-5 substituents selected from halo, cyano, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -C(O)R12, -C(O)OR12, --OC(O)R12, -NR12C(O)R13, -C(O)NR12R13, -NR12R13, hydroxy, 1-6C alkyl, and 1-6C alkoxy);

j = 0-2;
R12, R13 = H or 1-6C alkyl; and
R14 = R11, but not H;
ACTIVITY - Cytostatic.
MECHANISM OF ACTION - Inhibitors of the erbB family of oncogenic and protooncogenic protein tyrosine kinases.
USE - (I) are useful in the treatment of hyperproliferative disorders such as cancers.
Dwg.0/0

L44 ANSWER 5 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-422931 [36] WPIDS
DNC C2000-127931
TI Production of sertraline hydrochloride Form V used for treating e.g. depression by dissolving sertraline hydrochloride in solvent, removing solvent and drying.
DC **B05**
IN ARONHEIM, J; LIBERMAN, A; MENDELOVICI, M; NIDAM, T; SCHWARTZ, E; SINGER, C; VALDMAN, E
PA (TEVA-N) TEVA PHARM IND LTD; (TEVA-N) TEVA PHARM USA INC
CYC 90
PI WO 2000032551 A1 20000608 (200036)* EN 63p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000016336 A 20000619 (200044)
ADT WO 2000032551 A1 WO 1999-US27881 19991124; AU 2000016336 A AU 2000-16336 19991124
FDT AU 2000016336 A Based on WO 200032551
PRAI US 1999-147888 19990809; US 1998-110113 19981127; US 1999-125172 19990319; US 1999-133117 19990507
AB WO 200032551 A UPAB: 20000801
NOVELTY - Production of sertraline hydrochloride Form V comprises:
(1) dissolving sertraline hydrochloride in a **solvent**;
(2) removing the **solvent** and
(3) drying the sertraline hydrochloride Form V.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(i) production of sertraline hydrochloride Form V which comprises dissolving or suspending sertraline base in a **solvent**, adding hydrogen chloride or hydrochloric acid and isolating sertraline hydrochloride Form V;
(ii) production of sertraline hydrochloride Form V which comprises drying sertraline hydrochloride ethanolate Form VI, sertraline hydrochloride Form VII or sertraline hydrochloride hydrate Form VIII;
(iii) production of sertraline hydrochloride Form V which comprises suspending or dissolving sertraline hydrochloride in ethanol, methanol and/or water and isolating sertraline hydrochloride Form V;
(iv) production of sertraline hydrochloride Form V which comprises dissolving sertraline hydrochloride Form VI in water, adding hydrochloric acid or hydrogen chloride to facilitate precipitation of sertraline hydrochloride Form V, removing water and isolating sertraline hydrochloride Form V;

(v) production of sertraline hydrochloride Form V which comprises heating amorphous sertraline hydrochloride to effect transformation to Form V and isolating sertraline hydrochloride Form V;

(vi) sertraline hydrochloride Form VI, its ethanolate and methanolate;

(vii) production of sertraline hydrochloride Form VI which comprises dissolving sertraline base in a **solvent**, adding hydrogen chloride gas to the solution and isolating sertraline hydrochloride Form VI without further drying;

(viii) production of sertraline hydrochloride Form VI which comprising dissolving sertraline hydrochloride in ethanol or methanol, stirring to allow transformation to Form VI and isolating sertraline hydrochloride Form VI;

(ix) sertraline hydrochloride Form VII;

(x) production of sertraline hydrochloride Form VII which comprises suspending Form V in water and filtering the suspension without drying;

(xi) production of sertraline hydrochloride Form VII which comprises dissolving sertraline hydrochloride ethanolate Form VI in water to convert it to Form VII, filtering the Form VII and washing the filtered Form VII with water;

(xii) production of sertraline hydrochloride Form VII which comprises dissolving sertraline hydrochloride ethanolate Form VI in water, heating the solution to facilitate dissolution and isolating Form VII without drying;

(xiii) sertraline hydrochloride Form VIII;

(xiv) production of sertraline hydrochloride Form VIII which comprises suspending sertraline base in water, adding hydrochloric acid and filtering the precipitate without further drying;

(xv) production of sertraline hydrochloride Form VIII which comprising dissolving sertraline hydrochloride ethanolate Form VI in water and isolating Form VIII;

(xvi) production of sertraline hydrochloride Form VIII which comprises dissolving sertraline hydrochloride Form II in water and isolating Form VIII;

(xvii) sertraline hydrochloride Form IX;

(xviii) production of sertraline hydrochloride Form IX which comprises suspending sertraline base in water, adding hydrochloric acid, filtering the precipitate and drying the precipitate;

(xix) production of sertraline hydrochloride Form IX which comprises drying Form VIII and isolating Form IX;

(xx) sertraline hydrochloride Form X;

(xxi) production of sertraline hydrochloride Form X which comprises suspending sertraline hydrochloride in benzyl alcohol, heating the suspension to facilitate dissolution, cooling the solution to form a precipitate, heating the solution to 80 deg. C and isolating Form X;

(xxii) production of sertraline hydrochloride Form II which comprises suspending Form VI in an organic **aprotic solvent** to allow transformation to Form II and filtering the suspension;

(xxiii) production of sertraline hydrochloride Form II which comprises suspending Form V in dimethylformamide or cyclohexanol, heating the solution to effect transformation to Form II and isolating Form II;

(xxiv) production of sertraline hydrochloride Form II which comprises

dissolving sertraline base in acetone, adding hydrogen chloride solution to induce formation of Form II and isolating Form II;

(xxv) production of sertraline hydrochloride Form II which comprises granulating sertraline hydrochloride Form V with ethanol and stirring to induce transformation to Form II;

(xxvi) production of a mixture of Form II and Form V which comprises heating Form VI at upto 1 atmosphere pressure and isolating the mixture of

Form II and Form V;

(xxvii) production of sertraline hydrochloride Form III which comprises heating Form V to induce transformation to Form III and isolating Form III;

(xxviii) production of sertraline hydrochloride Form III which comprises heating Form VI to induce transformation to Form III and isolating Form III;

(xxix) production of amorphous sertraline hydrochloride which comprises suspending or dissolving sertraline base in a non-polar organic solvent, adding gaseous hydrogen chloride and isolating amorphous sertraline hydrochloride and

(xxx) production of amorphous sertraline hydrochloride which comprises lyophilisation of sertraline hydrochloride and isolating amorphous sertraline hydrochloride.

ACTIVITY - Antidepressant.

MECHANISM OF ACTION - None given.

USE - Sertraline hydrochloride is useful for treating depression, obsessive-compulsive disorder and panic disorder.

Dwg.0/16

L44 ANSWER 6 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-412264 [35] WPIDS
DNC C2000-124991
TI Production of cyclene for use in nuclear resonance tomography as a ligand for gadolinium comprises reacting triethylenetetramine with glyoxal, an alkylating agent and hydrazine hydrate.
DC **B04** E13 E33 J04
IN GRASKE, K; HOYER, K; PLATZEK, J; RADUECHEL, B
PA (SCHD) SCHERING AG
CYC 79
PI WO 2000032581 A1 20000608 (200035)* DE 21p
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE
W: AE AL AU BA BB BG BR CA CN CR CU CZ DM EE GD GE GH GM HR HU ID IL IN IS JP KE KP KR LC LK LR LS LT LV MA MG MK MN MW MX NO NZ PL RO SD SG SI SK SL TR TT TZ UA UG UZ VN YU ZA ZW
DE 19856481 C1 20000706 (200035)
AU 2000016543 A 20000619 (200044)
US 6156890 A 20001205 (200066)#
ADT WO 2000032581 A1 WO 1999-EP9089 19991117; DE 19856481 C1 DE 1998-19856481 19981202; AU 2000016543 A AU 2000-16543 19991117; US 6156890 A Provisional US 1999-116230 19990115, US 1999-451702 19991201
FDT AU 2000016543 A Based on WO 200032581
PRAI DE 1998-19856481 19981202; US 1999-451702 19991201
AB WO 200032581 A UPAB: 20000725
NOVELTY - Cyclene (I) is prepared in a one-pot process comprising:

(a) reacting triethylenetetramine (II) with 40% glyoxal;

(b) alkylating the secondary amino nitrogens of the resulting compound using a 1,2-difunctionalized alkylating agent (III);

(c) treating the condensation product with hydrazine hydrate (IV);
(d) liberating (I) from the cyclene salt; and
(e) isolating (I).
DETAILED DESCRIPTION - One-pot preparation of (I) comprises:
(a) reacting triethylenetetramine (II) with 40% glyoxal at 20-80 deg.
C in a polar protic **solvent** for 4-20 hours;
(b) after removing the **solvent**, alkylating both **secondary** amino nitrogen atoms of the resulting intermediate tricyclic compound by reaction with a 1,2-difunctionalized alkylating agent of formula (III) in a polar **aprotic solvent**, optionally in the presence of a base, at 20-120 deg. C for 2-24 hours;
(c) after removing the **solvent**, treating the resulting condensation product with hydrazine hydrate (IV), in a polar protic **solvent**, at pH 3-6 and at reflux temperature, for 12-48 hours;
(d) liberating (I) from the cyclene salt by treatment with a base; and
(e) isolating (I) after evaporation of the reaction **solvent**.
X(CH2)2X (III)
X = a nucleofugic group.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - (I) is useful as a starting material for the preparation of macrocyclic complexing agents and may also be used in nuclear resonance tomography as a ligand for gadolinium.
ADVANTAGE - Isolation of the various reaction intermediates is not required, so savings of time and material costs are achieved. The reaction with hydrazine hydrate does not generate significant amounts of by-products. The materials used in the process are cheap and readily accessible, and the process does not produce large quantities of waste. The total synthesis duration is short, and the process gives greater yields than prior art processes.
Dwg.0/0

L44 ANSWER 7 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-182535 [16] WPIDS
DNC C2000-057147
TI Obtaining a soluble cartilage component with anti-matrix metalloproteinase, antitumor, and antiangiogenic activities comprises treating cartilage with a solution containing organic solvent and separating off a mass of solids.
DC **B04**
IN AUGER, S; DUPONT, E; LACHANCE, Y; LESSARD, D
PA (AETE-N) LES LAB AETERNA INC
CYC 86
PI WO 2000004910 A2 20000203 (200016)* EN 58p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9948931 A 20000214 (200029)
US 6168807 B1 20010102 (200103)
ADT WO 2000004910 A2 WO 1999-CA674 19990723; AU 9948931 A AU 1999-48931

19990723; US 6168807 B1 US 1998-122481 19980723
FDT AU 9948931 A Based on WO 200004910
PRAI US 1998-122481 19980723
AB WO 200004910 A UPAB: 20000330
NOVELTY - Obtaining a soluble cartilage component with anti-matrix metalloproteinase (anti-MMP), antitumor, and antiangiogenic activities comprises treating cartilage with a solution containing organic solvent and separating off a mass of solids to obtain a soluble component.

DETAILED DESCRIPTION - A process (I) for obtaining a soluble component from cartilage comprises:

(a) treating cartilage material with a quantity of organic solvent-containing solution to form a first mixture comprising a soluble component of cartilage;

(b) separating the first mixture to form a first liquid extract comprising the soluble component and a first mass of solids, where the soluble component possesses one or more of anti-MMP, anti-tumor and anti-angiogenic activities.

INDEPENDENT CLAIMS are also included for the following:

(1) an improved process (II) for obtaining biologically active components from cartilage comprising:

(i) homogenizing cartilage in an aqueous solution until the average particle size of the cartilage is reduced to less than 500 microns to form a homogenate;

(ii) equilibrating the homogenate to extract the biologically active components into the aqueous solution and to form a first mixture comprising a first mass of solids and a first liquid extract containing the biologically active components;

(iii) separating the first liquid extract from the first mass of solids; and

(iv) subjecting said first liquid extract to a separation procedure to form a second liquid extract containing biologically active components having respective molecular weights less than 500 kDa; the improvement comprising:

(v) filtering the second liquid extract with a membrane having a nominal molecular weight cut-off of 1 kDa to form a filtrate comprising a first biologically active component having a molecular weight of less than 1 kDa and a retentate comprising a second biologically active component having a molecular weight 1-500 kDa, and where the first and second biologically active components possess at least an anti-MMP activity.

(2) a biologically active component obtainable from cartilage and possessing the following properties:

(a) a molecular weight less than 1 kDa;

(b) an anti-MMP activity.

(3) a first or second biologically active component prepared as in (1)

(4) a first biologically active component prepared as in (1) and further possessing anti-tumor activity;

(5) a first biologically active component prepared as in (1) where the cartilage material is shark cartilage and has a molecular weight of 244;

(6) a soluble component where the cartilage is shark cartilage, and which further possesses at least anti MMP activity, and at least one of antiangiogenic and anti-tumor activity and where the molecular weight is 244.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - MMP inhibitor.
USE - The soluble and biologically active components may be used to inhibit MMP, to inhibit neovascularization and formation of metastases in biological tissues and to treat angiogenesis related diseases, tumor related diseases and MMP related diseases in mammals (claimed).
Dwg.0/6

L44 ANSWER 8 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-180737 [15] WPIDS
DNC C1999-052673
TI **Parenterally** acceptable, non-toxic antifungal formulation - comprises pimaricin, useful against Fusarium, Aspergillus and Candida especially in immuno-compromised patients.
DC **B02 B03** C02
IN ANAISSIE, E J; ANDERSSON, B S
PA (TEXA) UNIV TEXAS SYSTEM
CYC 22
PI WO 9908663 A1 19990225 (199915)* EN 38p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP
US 6045815 A 20000404 (200024)
EP 1007013 A1 20000614 (200033) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9908663 A1 WO 1998-US16661 19980807; US 6045815 A US 1997-911607 19970815; EP 1007013 A1 EP 1998-939905 19980807, WO 1998-US16661 19980807
FDT EP 1007013 A1 Based on WO 9908663
PRAI US 1997-911607 19970815
AB WO 9908663 A UPAB: 19990416
NOVELTY - **Parenterally** acceptable, non-toxic formulation of pimaricin is new. DETAILED DESCRIPTION - Antifungal, **parenteral** composition comprises: (i) pimaricin (I) or its antifungal derivative effective to inhibit the growth of a systemic infection in a mammal; (ii) a dipolar **aprotic solvent**; and (iii) an aqueous **secondary solvent**.
MECHANISM OF ACTION - None given. ACTIVITY - antifungal.
USE - (I) is active against Fusarium and Aspergillus and Candida. The formulation may be used for cancer patients and other groups of immunocompromised patients, e.g. those suffering from HIV and those having recently undergone open heart surgery, all of which are targets for opportunistic infections. (I) has little or no toxicity after oral administration since (I) has been used in the food industry to prevent the proliferation of (aflotoxin-producing) moulds.
ADVANTAGE - (I) has low normal organ toxicity, high bioavailability and predictable pharmacokinetics after **parenteral** administration. (I) is non absorbable from the gastrointestinal tract due to its low solubility in both aqueous and organic **solvents**. The formulation allows **parenteral** administration of (I).
Dwg.0/15

L44 ANSWER 9 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-368174 [37] WPIDS
DNC C1996-116312
TI Aziridine ketone prepn., useful as medicine intermediate - comprises reacting beta-alkoxy amino ketone with base in at least e.g. polar or

ether solvent.
DC **B03**
PA (SUMO) SUMITOMO CHEM CO LTD
CYC 1
PI JP 08176103 A 19960709 (199637)* 6p
ADT JP 08176103 A JP 1994-322840 19941226
PRAI JP 1994-322840 19941226
AB JP 08176103 A UPAB: 19960918
Prepn. of aziridine ketone of formula (1) comprises reacting a beta-alkoxyaminoketone of formula (2) with base in at least **aprotic** polar **solvents**, ether **solvents** or aromatic **solvents**.
Also claimed are (A) prepn. of aziridine ketone of formula (1) by reacting alpha, beta-unsatd. ketone of formula (3) with O-alkylhydroxylamine of formula R5NHOR4 or its salt to form beta-alkoxyaminoketone of formula (2); and reacting with base in at least one **aprotic** polar **solvents**, ether **solvents** or aromatic **solvents**; and (B) prepn. of aziridine ketone of formula (1) by reacting alpha, beta-unsatd. ketone of formula (3) with O-alkylhydroxylamine of formula: R5NHOR4 or its salt in at least one **aprotic** polar **solvents**, ether **solvents** or aromatic **solvents**; and reacting with a base.
Pref. O-alkylhydroxylamine is O-methylhydroxylamine, O-ethylhydroxylamine, O-t-butylhydroxylamine, O-benzylhydroxylamine or N,O-dimethylhydroxylamine. Amt. of O-alkylhydroxylamine or its salt is 0.5-10 mole times to alpha,beta-unsatd. ketone. **Aprotic** polar **solvent** is DMF, **DMSO**, 1,3-dimethyl-2-imidazolidinone, N-methyl-2-pyrrolidone, sulpholane or hexamethylphophoramide. Ether **solvent** is THF, 2-methyltetrahydrofuran, tetrahydropyran, 1,4-dioxane etc. Amt. of base is 0.1-6 mole times to beta-alkoxyaminoketone.
Dwg.0/0

L44 ANSWER 10 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-277701 [28] WPIDS
DNC C1996-088147
TI Prepn. of 5-methoxycarbonyl-6-methyl-2-(((3,4-di methoxy-2-pyridinyl)methyl)sulphinyl)-1H-benzimidazol-1-yl methyl ethyl carbonate - used to inhibit gastric acid secretion for prevention and treatment of peptic ulcer.
DC **B02**
IN BRANDSTROM, A; BRAENDSTROEM, A
PA (ASTR) ASTRA AB
CYC 66
PI WO 9616959 A1 19960606 (199628)* EN 19p
RW: AT BE CH DE DK ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG UZ VN
AU 9641913 A 19960619 (199640)
ADT WO 9616959 A1 WO 1995-SE1414 19951127; AU 9641913 A AU 1996-41913 19951127
FDT AU 9641913 A Based on WO 9616959
PRAI SE 1994-4192 19941202
AB WO 9616959 A UPAB: 19960719
A process for the prepn. of 5-methoxycarbonyl-6-methyl-2-(((3,4-dimethoxy-

2- pyridinyl)methyl)sulphinyl)-1H-benzimidazol-1-ylmethyl ethyl carbonate and the single enantiomers thereof comprises reaction of an isomeric mixt. of two cpds. of formula (I), (Ia) or (Ib) with a nucleophile in a **solvent**. The 5-isomer is isolated from the reaction mixt. (Ia) (+)-enantiomers; (Ib) (-)-enantiomers. Also claimed is 5-carboxymethyl-6-methyl-2-(((3,4-dimethoxy-2-pyridinyl)methyl)sulphinyl)-1H-benzimidazol-1-ylmethyl ethyl carbonate prepd. by the process.

PREFERRED NUCLEOPHILE - The nucleophile has the formula RSH. R = opt. substd. 1-12C alkyl or opt. substd. aryl. Esp. R = 1-5C alkyl (opt. substd. with OH, carboxy, amino or amido) or phenyl. Esp. the nucleophile is e.g. thiophenol sodium salt, ethanethiol sodium salt, most esp. e.g. 2-mercaptoethanol. The **solvent** is a dipolar **aprotic solvent**, esp. **dimethyl sulphoxide**. The reaction is performed in the presence of a base, esp. a bicarbonate.

USE - 5-carbomethoxy-6-methyl-2-(((3,4-dimethoxy-2-pyridinyl)methyl)sulphinyl)-1H-benzimidazole-1-ylmethyl ether carbonate and the single enantiomers thereof inhibit exogenously or endogenously stimulated gastric acid secretion so can be used in the prevention and treatment of peptic ulcer.

ADVANTAGE - None given.

Dwg.0/0

L44 ANSWER 11 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-293563 [36] WPIDS
CR 1996-009547 [51]
DNC C1994-133839
TI Chiral 3-aminoalkyl-pyrrolidine deriv. prepn. - from 3-hydroxy cpd. via 3-sulphonate and 3-cyano cpds., useful as intermediate for antibacterials.
DC **B03**
IN FEDIJ, V; WEMPLE, J N; ZELLER, J R; SUTO, M J
PA (WARN) WARNER LAMBERT CO
CYC 28
PI US 5347017 A 19940913 (199436)* 6p
WO 9501962 A1 19950119 (199509) EN 25p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA CZ FI HU JP KR NO NZ RU SK
AU 9472172 A 19950206 (199518)
ADT US 5347017 A US 1993-88464 19930707; WO 9501962 A1 WO 1994-US7471 19940630; AU 9472172 A AU 1994-72172 19940630
FDT AU 9472172 A Based on WO 9501962
PRAI US 1993-88464 19930707
AB US 5347017 A UPAB: 19960115
Prepn. of chiral 3-(1-amino-1,1-bis-(alkyl)- methyl)-1-substd. pyrrolidines of formula (I) comprises: (1) reacting a chiral 1-(R1)-3-pyrrolidinol (II) with an alkylsulphonyl halide or arylsulphonyl halide in the presence of a base in an **aprotic solvent** ; (2) reacting the obtd. chiral 1-(R1)-3-pyrrolidinol sulphonate ester (III) with a cyanide reagent in an **aprotic solvent** ; and (3) reacting the obtd. chiral 3-cyanopyrrolidine (IV), having the opposite configuration from (III), with an excess of alkyl lithium in presence of a Lewis acid in an **aprotic solvent**. In the formula, R1 = benzyl, p-methoxybenzyl, alpha-methylbenzyl (opt. in optical

isomer form), OMe, OEt or NMe2; and R = 1-3C alkyl.

Also claimed are prepns. of (I) by either steps (2) and (3), or by step (3) only.

Pref., in step (1), the sulphonyl halide is e.g. MeSO2Cl, EtSO2Br. The base is an amine, pref. pyridine, quinuclidine, EtN(iPr)2 or esp. NEt3 or diazabicycloundecene. The **solvent** is e.g. toluene, CH2Cl2.

In step (2), the cyanide is an alkali metal cyanide used in presence of a phase transfer catalyst, or is itself a phase transfer reagent. The phase transfer catalyst or reagent is e.g. NBu4HSO4, NBu4CN, or trioctylpropylammonium cyanide. The **solvent** is e.g. DMF, **DMSO**.

In step (3), the **solvent** is e.g. THF, Et2O.

Esp. (II) is reacted with MeSO2Cl in presence of NEt3; (III) is reacted with NBu4CN in MeCN; and (IV) is reacted in the presence of MeLi or EtLi.

USE - (I) are key intermediates for naphthyridine or quinolone antibacterial agents, e.g. as described in US5072001 and US5157128.

ADVANTAGE - Starting materials (II) are easily and cheaply obtainable from D- or L-malic acid. (I) are obtd. economically in high yield. Step (3) proceeds without racemisation and with retention of configuration. Dwg.0/0

L44 ANSWER 12 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-163902 [20] WPIDS
DNC C1994-075007
TI Purificn. of bis maleimide(s) useful as starting materials for pharmaceuticals, pesticides etc. - by dissolving crude cpd. in **aprotic** polar **solvent** and pouring into water.
DC A41 **B03** C02 E13
PA (MITK) MITSUI TOATSU CHEM INC
CYC 1
PI JP 06107629 A 19940419 (199420)* 4p
JP 3085611 B2 20000911 (200046) 4p
ADT JP 06107629 A JP 1992-258002 19920928; JP 3085611 B2 JP 1992-258002 19920928
FDT JP 3085611 B2 Previous Publ. JP 06107629
PRAI JP 1992-258002 19920928
AB JP 06107629 A UPAB: 19940705
Purificn. of bismaleimides of formula (I) comprises (1) dissolving (I) or crude (I) compsn. into **aprotic** polar **solvent** (II); and (2) pouring the above soln. into water or specific organic **solvent** (III) to crystallise (I). In the formulae, X = bond, 1-10C bivalent hydrocarbyl, hexafluoroisopropylidene, carbonyl, thio or sulphonyl. Y1-Y4 = H, lower alkyl, lower alkoxy, Cl or Br.

(I) or its crude compsn. is prepd. by condensation of diamines with maleic anhydride in the presence of p-toluenesulphonic acid, dissolved in one or more of DMF, 2-methylpyrrolidone, N,N-**dimethylacetamide**, 1,3-dimethyl-2-imidazolinone and the soln. is poured into one or more of water, methanol or ethanol to crystallise (I) selectively.

USE/ADVANTAGE - (I) are useful as starting materials for drugs, pesticides or imide resins or laminates due to their heat resistance, stability and insulating properties. By the present procedure, acid catalyst (e.g. p-toluenesulphonic acid) is removed quite efficiently to obtain high quality (I) which are also used as electronic parts starting material.

Dwg.0/0

L44 ANSWER 13 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1993-288343 [36] WPIDS
DNC C1993-128697
TI Sepn. of high optical purity folinic acid stereoisomers - by selective crystallisation of new or known diastereomer salt with di- or poly-amine e.g. ethylene di amine.
DC **B02**
IN FELDER, E; PIVA, R; RIPA, G; FEKDER, E
PA (BRAC) BRACCO SPA; (BRAC-N) BRACCO SPA
CYC 20
PI WO 9317022 A1 19930902 (199336)* EN 34p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: JP KR US
EP 626965 A1 19941207 (199502) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI NL PT SE
ES 2065299 T1 19950216 (199513)
JP 07506813 W 19950727 (199538) 8p
IT 1254635 B 19950928 (199614)
US 5599931 A 19970204 (199711) 7p
EP 626965 B1 19980701 (199830) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI NL PT SE
DE 69319420 E 19980806 (199837)
ADT WO 9317022 A1 WO 1993-EP361 19930216; EP 626965 A1 EP 1993-903973 19930216, WO 1993-EP361 19930216; ES 2065299 T1 EP 1993-903973 19930216; JP 07506813 W JP 1993-514507 19930216, WO 1993-EP361 19930216; IT 1254635 B IT 1992-MI367 19920220; US 5599931 A Cont of US 1994-290812 19940817, US 1995-456767 19950601; EP 626965 B1 EP 1993-903973 19930216, WO 1993-EP361 19930216; DE 69319420 E DE 1993-619420 19930216, EP 1993-903973 19930216, WO 1993-EP361 19930216
FDT EP 626965 A1 Based on WO 9317022; ES 2065299 T1 Based on EP 626965; JP 07506813 W Based on WO 9317022; EP 626965 B1 Based on WO 9317022; DE 69319420 E Based on EP 626965, Based on WO 9317022
PRAI IT 1992-MI367 19920220
AB WO 9317022 A UPAB: 19960308
Sepn. of the (6R) and (6S)-diastereomers of folinic acid (FA), with recovery of prod. of high optical purity in free or salified form, comprises: (a) reacting racemic FA, in free or alkaline earth metal (AEM) salt form, in a liq. medium contg. at least one of dipolar **aprotic** organic **solvents**, water and water-soluble protic organic **solvents**, with an aliphatic acyclic or cyclic amine (I) contg. at least two amino gps. connected by at least one opt. substd. 2-3C hydrocarbon chain, to give a racemic FA-(I) salt; (b) crystallising the salt from soln. in a mixt. of water and a water-sol. dipolar **aprotic** organic solvnt, opt. contg. an organic water-sol. protic organic **solvent**, such that the first solid sepg. on cooling contains a major proportion of the (6R) or (6S) stereoisomer, the major proportion of the second isomer remaining in the crystallisation mother liquor; (c) purifying the isomer-enriched solid from (b) by one or more recrystallisations from the same **solvent** until the desired optical purity is reached and opt. converting the obtd. (I) salt into the corresp. AEM salt; and (d) diluting the mother liquor from step (b) with a dipolar **aprotic** and/or protic organic **solvent** and recrystallising the pptd. solid (contg. mainly the second isomer) as in

step (c), or treating the mother liquor, after evapn. of the organic **solvents**, with an excess of water-sol. AEM mineral salts and recrystallising the obtd. AEM salt of the second isomer one or more times from water until the desired optical purity is obtd..

USE/ADVANTAGE - More than 99% optically pure (6R) and (6S)-FA can both be isolated in high yield from the equimolar diastereomeric mixt. obtd. by chemical synthesis from folic acid. The process is industrially applicable. The (6S) isomer as calcium salt has (unspecified) pharmacological activity; the (6R) isomer is inactive.

Dwg.0/0

Dwg.0/0

L44 ANSWER 14 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1993-080345 [10] WPIDS
DNC C1993-035811
TI Mfg. 2,3,4,5-tetra fluoro benzoic acid useful as synthetic intermediate - by decarboxylation of tetra fluoro phthalic acid at 110-250 deg.C in non-reactive **aprotic solvent**.
DC **B05** C03 E14
PA (SDSB-N) SDS BIOTECH CORP
CYC 1
PI JP 05025084 A 19930202 (199310)* 4p
ADT JP 05025084 A JP 1991-206197 19910724
PRAI JP 1991-206197 19910724
AB JP 05025084 A UPAB: 19931122

Prepn. of 2,3,4,5-tetrafluoro benzoic acid comprises decarboxylation of tetrafluoro phthalic acid at 100-250 deg.C in non-reactive **aprotic solvent** whose b.pt. is more than 110 deg.C. Also prepn. of 2,3,4,5-tetrafluorobenzoic acid involves decarboxylation of tetrafluorophthalic acid at 130-150 deg.C in sulfolane contg. less than 5 vol. % of water in the presence of alkali metal carbonate (mole ratio to tetrafluorophthalic acid is 0.05-0.25).

Pref. reaction temp. is 130-200 deg.C. Water may pref. be added. Alkali metal carbonate and/or alkali metal hydrogencarbonate (less than 1 eq. of tetraphthalic acid) is added as a catalyst in the reaction. Examples of the **solvent** are sulfolane, **2**,4-dimethylsulfolane, **DMSO**, dimethylsulphone, sulfolene, (iso)quinoline, 2,6-lutidine and 2,4,6-trimethylpyridine. The reaction is carried out for 30 mins - 8 hrs., pref. 1-2 hrs.

USE/ADVANTAGE - The method is safe, and 2,3,4,5-tetrafluoro benzoic acid is obtd. in high yield and purity.

In an example, to sulfolane (100ml) were added tetrafluorophthalic acid (23.8g), potassium carbonate (0.7g) and water (5g), and the whole was stirred and heated at 140 +/- 5 deg.C for 1.5 hrs. After the soln. was cooled to room temp., aq. NaOH (NaOH: 4.4g, water: 40ml) was added, and sulfolane was recovered by extn. using methylene chloride (200ml), followed by extn. 2 times. Conc. HCl was added to aq. layer to make the soln. pH 1, followed by extn. with toluene three times, and toluene soln. was stirred at 60-70 deg.C for 30 mins, to eliminate tetrafluorophthalic acid. The toluene layer was conc. to give 2,3,4,5-tetrafluorobenzoic acid as crude crystals, which were further purified by recrystallisation from water. yield : 89.2 %; purity : 98.69%; water : 0.13%; m.pt. : 82-83 deg.C

Dwg.0/0

L44 ANSWER 15 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1992-252138 [31] WPIDS
DNC C1992-112450
TI Furan 2,5-di carboxaldehyde prepn. - by heating sugar in **di methyl-sulphoxide**, and removing water with **second solvent**.
DC A41 **B03** E13
IN GASET, A; RIGAL, L; SRI, H
PA (FURC-N) FURCHIM SRL
CYC 1
PI FR 2669636 A1 19920529 (199231)* 18p
ADT FR 2669636 A1 FR 1990-14833 19901122
PRAI FR 1990-14833 19901122
AB FR 2669636 A UPAB: 19931006
Furan 2,5-dicarboxaldehyde (I) is prepared by the following process: a) one or more sugars is mixed with i. a strongly polar **aprotic solvent** having a sulphoxide group, and ii. **another solvent** selected from diethyl ketone, methyl isobutyl ketone, dichloromethane, and ethyl acetate, b) the mixture is heated to convert the hydroxy methyl furfural (II) formed into (I). c) Water is added to create an aqueous phase which dissolves the sulphoxide **solvent** and d) the two phases are separated, the non-aqueous phase, containing the
(I) is recovered. e) This phase is concentrated by evaporation of the **solvent** ii. f) (I) is allowed to crystallise out, and is filtered off.
USE/ADVANTAGE - (I) is useful as a monomer in the synthesis polyamides and polyurethanes, and is also useful in the synthesis of pharmaceutical macrocycles. The process gives very good yields of pure productrat
0/1

L44 ANSWER 16 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-252137 [31] WPIDS
DNC C1992-112449
TI Hydroxymethyl furfural prepn. - by heating fructose in **di methyl sulphoxide** and purifying with water and solvent.
DC A41 **B03** C02 E13
IN GASET, A; MBAZOA, C; RAYMOND, F; RIGAL, L
PA (FURC-N) FURCHIM SRL
CYC 1
PI FR 2669635 A1 19920529 (199231)* 20p
ADT FR 2669635 A1 FR 1990-14832 19901122
PRAI FR 1990-14832 19901122
AB FR 2669635 A UPAB: 19931006
Hydroxy methyl furfural (I) is prepared by the following process: a) one or more sugars are mixed with an **aprotic**, strongly polar sulphoxide **solvent** and b) the mixt. is heated and cooled. c) Water is added so that the wt. of water is 0.2 - 5 times the wt. of the sulphoxide **solvent**, and then d) a **second solvent** is added, selected from dichloromethane, methyl isobutyl ketone, diethyl ketone, and diethyl ether, until the wt. of this **second solvent** is 0.2 - 5 times the wt. of the mixt.. This gives a second phase in which the (I) dissolves. e) The two phases are sepd. and that contg. (I) is kept and f) connected by evaporation of the **solvent**. g) The concentrated liq. is cooled and (I) crystallises and is filtered off.
USE/ADVANTAGE - (I) is an intermediate for several monomers used in

polymer synthesis and for certain pharmaceutical products, and it has an antifungal activity. This process gives good yields of pure product, does not require the use of catalysts, and is cheap to carry out as the **solvents** used can be recycled.
0/1

L44 ANSWER 17 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-168707 [21] WPIDS
DNC C1992-077578
TI Prepn. of alpha-glycero phosphoryl choline - by reacting prod. of isopropylidene-**glycerol** and 2-chloro-2-oxa-3,3,2-di oxo phospholane with tri methylamine, etc..
DC **B05**
IN PURICELLI, L
PA (MGIS) MAGIS FARM SPA
CYC 7
PI EP 486100 A1 19920520 (199221)* EN 6p
R: BE DE ES FR GB IT NL
IT 1245736 B 19941014 (199511)
ADT EP 486100 A1 EP 1991-202922 19911109; IT 1245736 B IT 1990-22069 19901115
PRAI IT 1990-22069 19901115
AB EP 486100 A UPAB: 19931006
Prepn. of alpha glycerolphosphorylcholine comprises (a) reacting isopropylidene-**glycerol** of formula (III) at 0-10 deg. C in an **aprotic solvent** with **2**-chloro-**2**-oxa-3,3,2-dioxyaphospholan of formula (II) to obtain isopropylidene 3-glyceryl-ethylenecyclic phosphate of formula (IV); (b) reacting the obtd. cpd. with trimethylamine in **aprotic solvent** at ambient temp. to obtain alpha isopropylidene 3-glycerophosphoryl choline of formula (V); (C) hydrolysing the cpd. obtd. in (b) in an acid aq. soln., purifying the alpha-glycerophosphorylcholine by elution through a column and crystallising it.
Step (a) is pref. carried out in ethyl ether, in the presence of an acid acceptor, pref. a tert. amine, partic. NEt3. (IV) is sepd. from the reaction mixt. by evaporating the **solvent** after elimination of tert. base salts. Step (b) is pref. carried out in CH2Cl2. Hydrolysis in step (c) is pref. carried out with aq. 0.1N HCl soln. (I) is purified by passing through a cationic resin of IRC-50 type, and is pref. crystallized from EtOH. (I) is obtd. in optically active levoratory, dextrorotary or racemic form starting respectively from D, L or racemic (III).
USE/AVANTAGE - (I) are useful as adjuvants in dyslipemia and in the prevention and treatment of atherosclerosis. The new process provides (I) in high yield (50-90% for each step) and high purity. (0/0)
0/0

L44 ANSWER 18 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-092891 [12] WPIDS
DNC C1992-042909
TI New base material for cell culture, for metabolic prods. - comprises uniform film of polyamide modified by di ketene treatment, for high cell adhesion and growth rate.
DC A23 A96 **B04** D16
PA (YAWA) NIPPON STEEL CORP
CYC 1
PI JP 04036182 A 19920206 (199212)* 3p
ADT JP 04036182 A JP 1990-138397 19900530

PRAI JP 1990-138397 19900530
AB JP 04036182 A UPAB: 19931006
Material comprises porous or uniform film of polyamide(s) modified by treatment with diketene. Polyamide pref. contains monomer units of formula
(I) (R is H, CH3 or C2H5). Polyamide is pref. heat-resistant aromatic. Polyamide with units (I) with R = H e.g. has glass transition temp. of 380
deg. C and decomposition temp. of 455 deg. C.. Polyamides are soluble in **aprotic** polar **solvents**, eg. N-methyl-2
-pyrrolidone, N,N-**dimethyl acetamide** and **DMSO**
forming porous uniform film. Film opt. comprises hollow thread. Modification is by reacting diketene with powder or formed film of polyamide. **Solvents** for reaction are e.g. addn. inactive with diketene, eg. hexane, heptane and dioxane. Deg. of modification is easily controlled by mol. ratio, reaction time and basic catalyst, e.g. trimethylamine.
USE/ADVANTAGE - Useful for research and prodn. of metabolic prods..
0/0

L44 ANSWER 19 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-363130 [49] WPIDS
DNC C1990-157772
TI New imidazo quinoxalinone(s) and aza analogues - have inodilatory, vasodilatory and venodilatory effects for treatment of angina, hypertension, etc..
DC **B02**
IN DAVEY, D D
PA (BERL-N) BERLEX LAB INC
CYC 15
PI EP 400583 A 19901205 (199049)* 21p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
US 5055465 A 19911008 (199143) 9p
US 5166344 A 19921124 (199250) 9p
EP 400583 B1 19991117 (199953) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69033355 E 19991223 (200006)
ES 2138956 T3 20000201 (200013)
ADT EP 400583 A EP 1990-110191 19900529; US 5055465 A US 1989-359182 19890531;
US 5166344 A Div ex US 1989-359182 19890531, US 1991-762144 19910919; EP 400583 B1 EP 1990-110191 19900529; DE 69033355 E DE 1990-633355 19900529, EP 1990-110191 19900529; ES 2138956 T3 EP 1990-110191 19900529
FDT US 5166344 A Div ex US 5055465; DE 69033355 E Based on EP 400583; ES 2138956 T3 Based on EP 400583
PRAI US 1989-359182 19890531
AB EP 400583 A UPAB: 19930928
Cpds. (I) and their salts are new where A = N or CH; B = NCR3; D = N or CR2; R, R1 = independently H, OH, lower alkyl or alkoxy, phenyloxy, -S(O)n-R6, -Q-Alk-W, -N(R7)2, 1-pyrrolidinyl or gps. (i)-(v). R2 = H, lower alkyl; phenyl or phenalkyl opt. substd. by 1-3 methoxy gps.; alkyl substd. by pyridinyl, or gps. (vi)-(viii) or pyridinyl; where R3 = H lower alkyl, phenyl, pyridinyl; or lower alkylphenyl or pyridinyl; R4, R5 = independently H or lower alkyl; R6 = lower alkyl, Ph. lower alkylphenyl or pyridinyl; R7 = independently H, lower alkyl, phenyl, pyridinyl or gps.
(ix) and (x). R8 = independently lower alkyl, Ph or pyridinyl; Q = O,

-NR9-, -CH2-O-, or -CH2-NR9-; w = OH, lower alkoxy, O-Ph, -N(R10)2, pyridinyl or gps. (xi)-(xiv) where R9 = H, lower alkyl or Ph; R10 = independently H, lower alkyl or Ph; R11 = independently H or lower alkyl; X = CH2, O, S(O)n, or -NR10-; n = 0-2; p = 0 or 1.

A number of cpds. are specifically claimed including 1-ethyl-8-(1H-imidazol-1-yl -3-methylimidazo a(1,5-a)quinoxalin-4-(5H)-one.

USE/ADVANTAGE - Cpds. (I) are positive inotropic vasodilators, mixed (arterial and venous) vasodilators and selective venodilators. They reduce both preload and afterload on the heart and are therefore useful in treatment of congestive heart failure. They are also used in treatment of angina pectoris, hypertension, and other circulatory disorders.

0/0

L44 ANSWER 20 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1989-310133 [43] WPIDS
DNN N1989-236244 DNC C1989-137281
TI Screening metal cpds. for super-oxide dismutase activity - by adding to mixt. of super-oxide anion source and radical scavenger, then recording ESR spectrum.
DC **B04** D16 J04 S03
IN DAMERAU, W; WISCHNEWSK, G
PA (DEAK) AKAD WISSENSCHAFTEN DDR
CYC 1
PI DD 268299 A 19890524 (198943)* 5p
ADT DD 268299 A DD 1988-312213 19880113
PRAI DD 1988-312213 19880113
AB DD 268299 A UPAB: 19930923

Determination of the superoxide dismutase (SOD) activity of metal complexes (I) comprises (1) dissolving (I) in an **aprotic solvent** of less than 10 vol.% water content together with a radical scavenger (II; spin trap cpd.); (2) separately dissolving a source of superoxide anion in the same, but anhydrous, **aprotic solvent**, opt. under protective gas and opt. with **addn.** of a **solvent** auxiliary; (3) mixing the two solns. and (4) measuring the ESR spectrum within a specified time (less than 5 min.). From the spectrum the SOD activity is evaluated semi-quantitatively by calibration against a material of known activity.

The **solvent** is **DMSO** and (II) is 5,5-dimethylpymoline-1-oxide (DMPO).

USE/ADVANTAGE - The method is used as a rapid screening procedure for potential pharmaceuticals (SOD mimics are useful for treating chronic inflammatory disorders of the joints). It is simpler than known processes and provides reliable comparison of SOD activity without interference from spontaneous dismutation reactions.

1/2

L44 ANSWER 21 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1988-186140 [27] WPIDS
DNC C1988-083019
TI N-substd. maleimide(s) prodn. - by reacting maleic anhydride with prim. amine in organic **solvent** azeotropic with water or

aprotic polar **solvent**.
DC **B03** E13
PA (NITT) NITTO CHEM IND CO LTD
CYC 1
PI JP 63122666 A 19880526 (198827)* 5p
JP 07072173 B2 19950802 (199535) 4p
ADT JP 63122666 A JP 1986-267777 19861112; JP 07072173 B2 JP 1986-267777 19861112
FDT JP 07072173 B2 Based on JP 63122666
PRAI JP 1986-267777 19861112
AB JP 63122666 A UPAB: 19930923
Maleic anhydride is reacted with aromatic or aliphatic primary amines in an organic **solvent** at 50-200 deg. C in opt. presence of an acid catalyst selected from oxyacid of sulfur or phosphorus and organic sulphonic acids and water is removed to give maleimides in a single process; organic **solvent** azeotropic with water selected from benzene, toluene, xylene, ethylbenzene and chlorbenzene, or **aprotic** polar **solvent** selected from formamide, DMF, **dimethylacetamide**, N-methylformamide, **DMSO**, sulfolane, gamma-butylactone and hexamethylsulphamide is used. Pref. prim. amines are aromatic amines (e.g. aniline, dimethylaniline, chloroaniline, dichloroaniline, phenylenediamine, etc.) and aliphatic amines (e.g. methylamine, ethylamine, ethylamine, propylamine, butylamine, ethylenediamine, etc.). (2) The amt. of the azeotropic **solvent** is the amount of the non-proton polar **solvent** is 2-30% of total **solvent**. (3) The acid catalyst is sulfuric acid, phosphoreic acid, methanesulfonic acid, benzene sulfonic acid, toluene sulfonic acid, etc. and additive amount is 0.1-20 (1-10 wt.%) of used amt. of maleic anhydride.
USE/ADVANTAGE - Prepn. of N-substd. maleimide useful as intermediates for medical and chemical products free from side-production of polymer and with high yield is provided.
0/0

L44 ANSWER 22 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1987-230766 [33] WPIDS
DNC C1987-097311
TI Sepn. of polyfluorinated aliphatic mono or poly-carboxylic acid - from its addn. prod. with **aprotic** amide cpd., using aq. soln. of mineral acid in presence of water immiscible organic **solvent**.
DC **B05** C03 E16
PA (TOYJ) TOYO SODA MFG CO LTD
CYC 1
PI JP 62153244 A 19870708 (198733)*
ADT JP 62153244 A JP 1985-292432 19851227
PRAI JP 1985-292432 19851227
AB JP 62153244 A UPAB: 19930922
Sepn. of polyfluorinated aliphatic mono or polycarboxylic acid of formula Rf(COOH)n (I) from addn. prod. consisting of the acid and **aprotic** amide cpd., is effected by treating the addn. prod. with aq. soln. of mineral acid in the presence of organic **solvent** immiscible with water and capable of dissolving at least the acid. In (I) Rf = 1-20C

(un)satd. opt. branched polyfluoroaliphatic gp.; n = 1 - bond numbers of Rf minus 2).

Aprotic amide **solvents** are pref. DMF, **dimethylacetamide**, N-methylpyrrolidone, etc. Organic **solvents** used for coexistence are ethers, esters, alcohols, halogenated hydrocarbons, etc., among which 4-10C ethers e.g. ethyl ether, isopropyl ether, or butyl ether are pref. Use amts. of the **solvents** are defined in such a way that concn. of Rf(COOH)n sepd. from the **addn.** prod. in the **solvents** comes to pref. 5-50 wt.%. Mineral acid used is pref. HCl, H2SO4, or HNO3, esp. HCl, concn. and use amt. of which are usually 1-10 moles/litre and pref. 1.5-fold equiv. to N atom constituting amide gp. of **aprotic** amide **solvent** in reaction system, respectively.

USE/ADVANTAGE - (I) are useful as surfactants, water- or oil-repellent agents, or intermediates for pharmaceuticals and agricultural chemicals. (I) are prepd. by reacting perfluoroaliphatic halides with Zn and CO2 in the presence of **aprotic** amide **solvents**. In that case, (I) are obtd. as stable addn. prods. of 1:1 ratio with **aprotic** amide cpds. used as **solvents** by hydrolysing intermediates in reaction liquor, with aq. soln. of mineral acid, as such or after removing **solvent** to some extent by distn. Decomposition of the addn. prods. to obtain (I) is difficult. The addn. prods. can be easily and completely decomposed by the present method conducting acid-treatment with coexistence of organic **solvent**. (I) is extracted at high recovery rate by the **solvent**.

0/0

L44 ANSWER 23 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1986-341367 [52] WPIDS
DNC C1987-065779
TI **Parenteral** grade sodium amoxycillin prodn. - from tri hydrate, by suspending in solvent mixt., solubilising with amine then pptn. with sodium carboxylate.
DC **B02**
PA (ANTI-N) ANTIBITICOS SA
CYC 17
PI ES 8606871 A 19861016 (198652)* 16p
EP 220925 A 19870506 (198718) EN
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
AU 8664233 A 19870430 (198723)
ZA 8607982 A 19870511 (198734)
US 4737585 A 19880412 (198817)
CA 1272189 A 19900731 (199036)
AU 9068576 A 19910509 (199126)#
ADT ES 8606871 A ES 1985-548089 19851021; EP 220925 A EP 1986-308187 19861021;
AU 8664233 A AU 1986-64233 19861021; ZA 8607982 A ZA 1986-7982 19861021;
US 4737585 A US 1986-921105 19861021
PRAI ES 1985-548089 19851021
AB ES 8606871 A UPAB: 19930922
Prepn. of sodium amoxycillin (I) for **parenteral** admin. comprises (1) suspending amoxycillin trihydrate (II) in a mixt. of **aprotic** organic **solvent** and lower alcohol; (2) solubilising (II) by adding low mol. wt. cyclic or heterocyclic amin, then (3) adding Na diethyloxalsacetate (IIIa) or Na 2-ethylhexansate (IIIb). The mixt. was

stirred at -10 deg.C to room temp., then (I) pptd. by adding **aprotic** organic **solvent** and filtered off.

The **aprotic solvent** is MeCN, CH2Cl2, CHCl3 or 1,2-dichloroethane, and the alcohol is MeOH, EtOH, n-or iso-propanol, or n-or iso-butanol.

USE-ADVANTAGE - (I) is known as a broad-spectrum antibiotic. It is now recovered more economically (by pptn. and filtration) compared to the convetional **lyophilisation** procedure. (First major country equivalent to ES8606871-A)

0/0

L44 ANSWER 24 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1986-240298 [37] WPIDS
DNC C1986-103336
TI Prepn. of dulofibrate - from p chloro phenol and halo-iso butyryl halide.
DC **B05**
IN DESCAS, P; FENIOU, C
PA (CORT-N) SOC CORTIAL SA
CYC 15
PI EP 194221 A 19860910 (198637)* FR 8p
R: BE CH DE GB IT LI LU NL
PT 82092 A 19860814 (198639)
FR 2577924 A 19860829 (198641)
JP 61263948 A 19861121 (198701)
US 4638082 A 19870120 (198706)
ES 8702334 A 19870316 (198716)
ZA 8601510 A 19870828 (198747)
EP 194221 B 19880608 (198823) FR
R: BE CH DE GB IT LI LU NL
DE 3660284 G 19880714 (198829)
CA 1254228 A 19890516 (198924)
ADT EP 194221 A EP 1986-450004 19860124; FR 2577924 A FR 1985-3094 19850228; US 4638082 A US 1986-832688 19860225; ES 8702334 A ES 1986-551927 19860213; ZA 8601510 A ZA 1986-1510 19860228
PRAI FR 1985-3094 19850228
AB EP 194221 A UPAB: 19930922
p-Chlorophenoxy isobutyric acid p-chloro phenol ester (dulofibrate) (I) is prepd. by salification of p-chlorophenol (II) in benzene, dioxan, xylene or toluene, and treating 2 or 3 moles of the resultant salt (III) with a halo isobutyric acid halide (IV).

USE/ADVANTAGE - (I) is a known agent for treating hyperlipemia. This new process is easier and cheaper to carry out than known methods.

0/0

L44 ANSWER 25 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1986-039693 [06] WPIDS
DNC C1986-016944
TI Anti-ulcer ether(s) prodn. - comprising reacting phenol with alkane having two leaving gps. in presence of base.
DC **B05**
PA (ELED) DENKI KAGAKU KOGYO KK
CYC 1
PI JP 60260533 A 19851223 (198606)* 4p
ADT JP 60260533 A JP 1984-94252 19840511
PRAI JP 1984-94252 19840511

AB JP 60260533 A UPAB: 19930922
Prodn. of ethers of formula (I) comprises reacting a phenol of formula (II) with a cpd. of formula Y(CH2)nZ (III) in presence of a base; X is H or dialkylamino which may form a ring; Y and Z are the same or different representing a leaving gp.; n is 3 or 4.
Pref. reaction is carried out in a **solvent**, e.g. alcohol (MeOH, EtOH), water, ether (THF, dioxane, 1,2-dimethoxyethane), **aprotic** polar **solvent** (DMFA, **DMSO**), in presence of a base, e.g. alkali metal hydroxide or carbonate (e.g. NaOH, KOH, Na2CO3), alkoxide (e.g. NaOMe, NaOEt), NaH, with stirring at 50-130 deg.C for 1-6 hrs.. For 1 mole of (II), 0.8-1.2 mole base and 0.8-3 mole (III) may be used.
USE/ADVANTAGE - (I) are useful as intermediates in prepn. of drugs, e.g. 1-(3-(3-isothiocyanatopropoxy) phenylmethyl) piperidine having anti-ulcer activity. Use of (I) reduces steps towards dug.
0/0

L44 ANSWER 26 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1985-318579 [51] WPIDS
DNC C1985-137590
TI Tri fluoromethyl acetic or-sulphonic acid prodn. - by reacting metal with carbon or sulphur di oxide di oxide, then treating with tri fluoromethyl halide.
DC **B05** C03 E16
IN TORDEUX, M
PA (RHON) RHONE-POULENC SPECI; (RHON) RHONE POULENC SPECIALITES CHIM
CYC 15
PI EP 165135 A 19851218 (198551)* FR 13p
R: AT BE CH DE FR GB IT LI LU NL SE
FR 2564829 A 19851129 (198603)
JP 61010529 A 19860118 (198609)
BR 8502411 A 19860121 (198610)
ES 8607919 A 19861116 (198704)
EP 165135 B 19880824 (198834) FR
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3564565 G 19880929 (198840)
CA 1251465 A 19890321 (198916)
JP 02004213 B 19900126 (199008)
JP 02042054 A 19900213 (199012)
JP 04063060 B 19921008 (199245) 5p
ADT EP 165135 A EP 1985-400955 19850515; FR 2564829 A FR 1984-8010 19840523; JP 61010529 A JP 1985-106228 19850520; ES 8607919 A ES 1985-543376 19850522; JP 02004213 B JP 1989-189018 19860716; JP 04063060 B Div ex JP 1985-106228 19850520, JP 1989-189018 19850520
FDT JP 04063060 B Based on JP 02042054
PRAI FR 1984-8010 19840523
AB EP 165135 A UPAB: 19930925
Prodn. of trifluoromethyl-substd. acids (I) comprises first reacting a metal (M) with CO2 and SO2 in a polar **aprotic solvent**, then in a **second** step adding a CF3- halide (A), opt. together with CO2 and/or SO2, at a pressure over 1 bar. (M = Zn, Al, Mn, Cd, Mg, Sn, Fe, Ni or Co). M is esp. Zn or Al (esp. in finely-divided form); (A) is CF3Br and the **solvent** is MeCN, hexamethylphosphortriamide, **dimethyl acetamide**, N-methylpyrrolidone, or pref. **DMSO** or DMF.
USE/ADVANTAGE - The method is esp. applied to make CF3COOH and CF3SO3H, which are useful as catalysts and as intermediates in synthesis

of pharmaceuticals and plant-protection agents. This process is less expensive than known methods which use electrochemical fluorination or CF3I.
0/0

L44 ANSWER 27 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1985-197499 [33] WPIDS
DNC C1985-086245
TI 3-Methyl-2-buten-4-olide prodn. - by co dimerisation of methylene-cyclopropane with carbon di oxide in presence of palladium cpds..
DC **B03** E13
IN BINGER, P; WEINTZ, H J
PA (STUD) STUDIENGESELLSCHAFT KOHLE MBH
CYC 13
PI DE 3403793 A 19850808 (198533)* 9p
EP 152027 A 19850821 (198534) DE
R: AT BE CH DE FR GB IT LI LU NL
JP 60248681 A 19851209 (198604)
US 4659843 A 19870421 (198718)
CA 1239411 A 19880719 (198834)
EP 152027 B 19900411 (199015)
R: AT BE CH DE FR GB IT LI LU NL
DE 3577090 G 19900517 (199021)
ADT DE 3403793 A DE 1984-3403793 19840203; EP 152027 A EP 1985-101035 19850201; JP 60248681 A JP 1985-19180 19850201; US 4659843 A US 1985-697354 19850201
PRAI DE 1984-3403793 19840203
AB DE 3403793 A UPAB: 19930925
Prodn. of 3-methyl-2-buten-4-olide (4-methyl-2(5H)-furanone). (I) by codimerisation of methylenecyclopropane (II) with carbon dioxide at a pressure of 10-110 bar and at 100-200 deg.C in the presence of palladium (O) cpds. which are stable in the reaction mixture at up to 200 deg.C, optionally in the presence of a **solvent**. The palladium (O) cpds. is pref. formed in situ. Reaction temp. is pref. 150-200 deg.C and pressure is pref. 30-80 bar. The reaction is pref. carried out in a polar **aprotic solvent**, e.g. **dimethylsulphoxide** or dimethylformamide. In a pref. procedure a solution of the catalyst (1-10 mmol/l) and (II) (2-5 mol/l) in the **solvent** is injected at a rate of 1-20 ml/min. without **additional** cooling into the **solvent**/CO2 mixture (200ml reaction volume).
USE/ADVANTAGE - (I) is of interest as an intermediate for natural products, e.g. alpha-tocopherol (cf. Helv.Chim. Acta 62,464 (1979)) and rose furan (the active constituent of Bulgarian)
rose oil) (cf. Tetrahedron Letters 1077, 4443). Smooth reaction giving up to 85% yield.
0/0

L44 ANSWER 28 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1984-226314 [37] WPIDS
DNC C1984-095461
TI 3-Alkylthio-2-O-carbamoyl-1,2-propane di ol 1-0-phospho-choline(s) - useful as medicaments and for liposome prodn..
DC **B05**
IN BETZING, H; LAUTENSCHL, H H; WINKELMANN, J
PA (NATW) NATTERMANN & CIE GMBH A
CYC 13

PI DE 3307924 A 19840906 (198437)* 21p
EP 118090 A 19840912 (198437) EN
R: AT BE CH DE FR GB IT LI LU NL SE
JP 59170098 A 19840926 (198445)
ZA 8401534 A 19840827 (198501)
EP 118090 B 19861105 (198645) EN
R: AT BE CH DE FR GB IT LU NL SE
DE 3461189 G 19861211 (198651)
ADT DE 3307924 A DE 1983-3307924 19830305; EP 118090 A EP 1984-102006 19840225; JP 59170098 A JP 1984-40616 19840305; ZA 8401534 A ZA 1984-1534 19840229
PRAI DE 1983-3307924 19830305
AB DE 3307924 A UPAB: 19930925
3-Alkylthio-2-O-carbamoyl-1,2-**propanediol** 1-O-phosphocholines of formula (I) are new. R1 = linear satd. or unsatd. 10-20C hydrocarbyl; R2 and R3 = linear or branched satd. or unsatd. 1-20C hydrocarbyl, phenyl (opt. substd. by 1-3C alkyl, 1-3C alkoxy, halogen or CF3), benzyl or H.
Pref. R1 = 16-18C n-alkyl; R2 = H, and R3 = 16-18C USE - (I) may be used to treat hypertension and rheumatic and atherosclerotic disorders and
for tumour therapy. They may also be used to prepare phospholipase-resistant liposomes.
0/0

L44 ANSWER 29 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1984-069511 [12] WPIDS
DNC C1984-029784
TI 2,2-Di substd. vinyl-ketone cpds. - produced by reaction of ketone(s) with
hetero cumulene(s) such as carbon di sulphide and alkylation of prod..
DC **B05**
IN RUDORF, W D
PA (AUGU-I) AUGUSTIN M
CYC 1
PI DD 204252 A 19831123 (198412)* 9p
ADT DD 204252 A DD 1982-238680 19820402
PRAI DD 1982-238680 19820402
AB DD 204252 A UPAB: 19930925
Cpds. of formula (I) are prepd. by reaction of ketones R1-CH2-CO-CH2-R2 (II) with a heterocumulene such as carbon disulphide or an isothiocyanate in an **aprotic solvent** with the **addn**. of a
base at 0 deg.C to room temp. and the resulting gem-dithiolate or amino-thiolate of formula (III) is alkylated with an equimolar amt. of an alkylating agent. R1 and R2 are H, alkyl or aryl; A is SNa or NH-R4; A' is
NHR4 or -SR3; each residue R3 is opt. substd. alkyl or the two gps. R3 are
linked so as to form a gp. -(CH2)n- in which n is 1, 2 or 3; and R4 is alkyl or aryl.
Suitable bases for use in the reaction of (II) with a cumulene are NaH and sodium tert-amylate, and suitable **solvents** include **DMSO**, benzene and DMF.
The prods. can be used as biologically active substances.
0/0

L44 ANSWER 30 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1983-05855K [03] WPIDS

DNC C1983-005790
TI 2-Azido-substd. unsatd. carboxylic acid derivs. prepn. - by reacting 2,3-di substd. carboxylic acid ester with sodium azide in **aprotic** polar **solvent**.
DC **B05** E19
PA (SAGA) SAGAMI CHEM RES CENTRE
CYC 1
PI JP 57197252 A 19821203 (198303)* 4p
PRAI JP 1981-81130 19810529
AB JP 57197252 A UPAB: 19930925
Prepn. of 2-azido-substd. unsatd. carboxylic acid derivs. of formula (I) R2CH=CN3-CO2R1 (I), useful as intermediates for amino acids which constitute physiologically active peptides, comprises reacting a 2,3-disubstd. carboxylic acid ester of formula (II) R2CHX-CHX-CO2R1 (II) with sodium azide in **aprotic** polar **solvent** (e.g. DMF, **DMSO**, HMPT, NMP, sulphoran, etc.). R1 is H, alkyl or aryl; R2 is H or alkyl; X is halogen, alkyl or arylsulphonyloxy.

Pref. sodium azide is used in amt. at least 1.5 equivs., pref. 2-4 equivs., based on (II). The reaction temp. is 0-200 deg.C, but since high temp. reaction is accompanied by decomposition of starting materials and the prod., 40-80 deg.C is pref. The reaction between (II) and sodium azide is conducted in water-ethanol **solvent** to give **2**,3-diazido- carboxylic acid esters.

(I) are produced in higher yields and with shorter reation steps as compared with conventional methods starting from the corresp. unsatd. carboxylic acid deriv. and involving 3 reaction steps.

L44 ANSWER 31 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1980-72133C [41] WPIDS
TI Para-hydroxy-benzyl cyanide prepn. - from para-hydroxy-mandelic acid and cyanide ion.
DC **B05**
IN COOPER, M J; COPELAND, R J; EDWARDS, P N
PA (ICIL) IMPERIAL CHEM IND LTD
CYC 1
PI GB 1576332 A 19801008 (198041)*
PRAI GB 1976-8067 19760301
AB GB 1576332 A UPAB: 19930902
Para-hydroxy-benzyl cyanide (I) is prepd. by reacting p-hydroxy-mandelic acid (II) with cyanide ion.

The cyanide ion is conveniently provided by an alkali metal cyanide e.g. NaCN or JCN. A suitable **solvent** is a relatively high boiling, dipolar, **aprotic solvent** such as DMF, **2**-pyrrolidone, N-methyl-2-pyrrolidone or **dimethyl sulphoxide**. Alternatively a lower boiling **solvent** may be used, e.g. methanol with or without 1,2-dimethoxyethane, pref. used in the presence of a formate.

On hydrolysis (I) is converted to p-hydroxyphenyl acetamide which is an intermediate in the prepn. of the beta-adrenergic blocking agent p-(2-hydroxy-3-isopropylaminopropoxy) phenyl acetamide.

L44 ANSWER 32 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1974-41478V [22] WPIDS
TI Monoalkanoyl fluoresceins prodn. - by reacting fluorescein and a higher alkanoyl halide in an **aprotic solvent**.

DC **B02**
PA (HOFF) HOFFMANN-LA ROCHE
CYC 9
PI US 3812153 A 19740521 (197422)*
BE 808167 A 19740604 (197425)
DE 2359099 A 19740612 (197425)
NL 7316275 A 19740607 (197425)
FR 2208895 A 19740802 (197440)
JP 49087735 A 19740822 (197443)
AT 7310144 A 19760215 (197610)
GB 1431470 A 19760407 (197615)
CH 589641 A 19770715 (197734)
PRAI US 1972-312386 19721205
AB US 3812153 A UPAB: 19930831
Prepn. of compounds of formula (I): (where n is 8-16) comprises reacting a
10-18C alkanoyl halide with fluorescein at 15 degrees-30 degrees C under anhydrous conditions in an inert atmosphere in an **aprotic** organic **solvent** selected from DMF, **DMSO** or hexamethyl phosphoric triamide, the reaction mixt., after completion, is neutralised with a basic material and the product isolated by filtering on an adsorbing filter medium (alumina or silica gel) then eluted with an aromatic **solvent**-ether mixt. contg. **2**-15 vol. of aromatic solventandl vol. of ether, and crystallising (I) from hexane.

(I) are useful in fluorometric methods for determining lipase activity of body fluids (I) are obtd. in sufficient purity and higher yields.